

Dicamba ESA Requirements w/ OPP & OECA	Multi-divisional Team Leader Mtg
	•Python CoP monthly webinar
•EFED ESA Public Meeting Webinar •Dicamba ESA requirements	•Managing EFED Models
	•Managing EFED Models •Multi-Divisional TL Mtg Reboot (EFED, Modeling etc)
•EFED Management •Sensitivity Analysis workshop	•All-Day LER Basics Supervisor Training •Community of Practice for Statistics June •Water Monitoring SAP •Pesticide Usage Meeting Conference

	<ul style="list-style-type: none"> •ESA QC Write-up ••ESA Team meeting 	
	<ul style="list-style-type: none"> •HED Residue Data and DWA Modeling 	
<ul style="list-style-type: none"> •EFED New Employee Training •EFED Pesticide Fate and Transport Technical Team Weekly Meeting •Methomyl/Carbaryl Team Meeting 	<ul style="list-style-type: none"> •TDD 2-32 Biweekly Meeting •EFED Plant Technical Team Bi-weekly Meeting 	

WEEK AT-A-GLANCE (WAAG)

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BRANCH	
IO	Stakeholder/Briefing
	Risk Assessment
	Registrant/Applicant/Tour
	SAP/CRP/EDSP
	Other OPP & Div. Meetings
	Other
ERB1	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
	Other
ERB2	Stakeholder/Briefing
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	Registrant
	Other

		6/7/19
Wednesday	Thursday	Friday
Each Wednesday EFED Director in S-7913		
ESA public meeting walk through presentations - for real dry run	Farm Bill ESA Interagency Working Group Meeting	
	Almond Board of CA	
RD/EFED General HED/EFED General	EFED/BEAD General	
DC Cir. Pests. Weekly Call		
-Thiamethoxam poultry litter EDWCs -Neonic off-week EFED meeting	-Folpet DRA kick-off -Neonic biweekly meeting w/ PRD	
Imazamox NU Meeting with RD		
	ESA Team Leads	
- Chlorpyrifos Team Meeting - Flonicamid New Uses RD Meeting - Neonics EFED Team Biweekly	Neonics Biweekly with PRD	
OPPEL Coordination Team Meeting	ESA Team Leads	
PMRA and Registrant - Bee Study Discussion Anticoagulant rodenticide kick-off		
EFED Off-Week Neonic Biweekly	Neonic Biweekly w/ PRD & BEAD	

ERB6	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
	Other
EISB	IT
	ESA
	Modeling
	Other
All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)

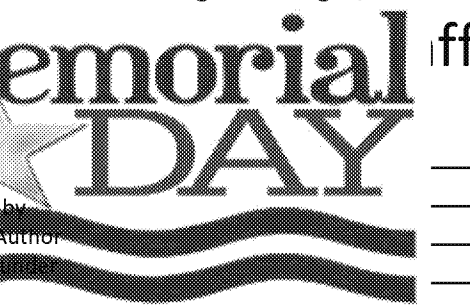
	Common Effects Check-in

EFED Off-Week Neonic Biweekly Anticoagulant Rodenticide EFED Kickoff	Neonic Biweekly w/ PRD & BEAD	

WEEK AT-A-GLANCE (WAAG)

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Tuesday	Wednesday
Pesticide Usage Meeting w/Services	Synergy Mtg at Hdqrs
	Lunch and Learn: BEAD Describes Pesticide Application Equipment (Field) and Exposure Considerations
	DC Cir. Pests. Weekly Call
	Neonic biweekly EFED meeting
	Methomyl/Carbaryl ESA
	Neonics Biweekly Team Meeting
	Methomyl/Carbaryl Team Meeting
Silver Nitrate New Uses w/ RD	EFED Neonic Biweekly
	PRD's DD Neonic Briefing
	EFED Neonic Biweekly Amicarbazone RR Kickoff w/ PRD
	SFIREG EPA Dicamba Ad hoc Workgroup

5/31/2019	
Thursday	Friday
Senior Science Advisor Forum	
ESA Team Meeting Norflurazon Registration Review team meeting	
Resources Meeting with ITRMD	
ESA Principals and Public Meeting Prep	
Indoor fumigant DRA meeting	
ESA Team Lead	
Halauxifen: RD New Uses Meeting	
Naphthalene: Mitigation Conference Call	
- ESA Team Leaders Meeting - WDA Regulator in Residence EFED Overview	
Tiafenacil Discussion with PMRA	
Fumigant Check in w/ PRD	
Aminocyclopyrachlor Planning w/ RD Norflurazon RR Mtg w/ PRD	

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Monday	Tuesday
Pyrethroids Registration Review Briefing	Pesticide Usage Mtg w/Services
Chlorpyrifos Bi-weekly	- Risk Assessment: Sulfoxaflor New Use - New Dicamba Innovations and Strategy to Move Forward
OPP Weekly Staff Meeting	EFED/PRD General
First Team Meeting: Sulfuric Acid	Cyproconazole Risk Overview with PRD
- Chlorpyrifos OD Biweekly Update - Fluoxastrobin DRA Kickoff Meeting	
	Fluroxypyr: Corteva Discussion on Compost Study for RR
	Pollinator Team Mtg
	EFED DD Briefing Sulfoxaflor
	Saflufenacil - Reg Rev 2 first team meeting follow up
	Permethrin - Multiple Action check in with RD
	CC with Corteva - Sulfoxaflor Sucrose Mixing
	Sulfoxaflor - w/RD pre-brief preparation

5/24/2019		
Wednesday	Thursday	Friday
	Senior Science Advisor Forum	
EFED DD Neonics Final RA Briefing DD briefing on sulfoxaflor	Initial Methiozolin Risk Assessment Brief DD briefing on sulfoxaflor	
	AMCA Meeting	
RD/EFED General	Resources Meeting	
	EFED/BEAD General	
Neonics Final RA: EFED DD Briefing		
	Neonics biweekly meeting w/ PRD	
	ESA Team Lead	
- Chlorpyrifos PRD Team Meeting - Neonics: EFED DDs Briefing	- Cyclaniliprole: RD New Uses Team Meeting - Neonics PRD Biweekly Meeting	
OPPEL Workgroup	ESA Team Leaders Meeting	
Thiencarbazone-methyl 1st Team Mtg Methomyl/Carbaryl Team Mtg		
Neonic RA Briefing for EFED DD	RD DD Briefing Sulfoxaflor	
Carbendazim DWLOC's with HED Ethoprop - Next steps with BEAD/PRD	Neonic Biweekly w/ PRD	
Neonic RA Briefing for EFED DD		
Flumetralin DRA Team Mtg w/ PRD	Neonic Biweekly w/ PRD	

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	ESA Usage Method
	Novices' Guide Meeting

	OPP Records Management Training	
	ESA Team Meeting	
	SAM Weekly/ Scenarios Project	
Methomyl/Carbaryl Team Meeting	Stats/ CETIS Team meeting	

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5/17/2019		
Wednesday	Thursday	Friday
	Sr. Science Advisor-Manager Forum Initial Methiozolin Risk Assessment Briefing	
Methomyl/Carbaryl Team Meeting		
	American Mosquito Control Assoc. Mtg ESA Team Meeting	
EFED/ITRMD General	Resources Meeting	
Neonic biweekly EFED meeting	Fumigant POC meeting w/ PRD	
Methomyl/Carbaryl Team Meeting	ESA Team Leads	
	American Mosquito Control Association	
	Uniconazole: PRD Team Meeting	
Presubmission (call) Meeting for Microencapsulated Insecticidal Paint		
OPPEL Coordination Group	ESA Team Leaders Meeting	
Methomyl/Carbaryl Team Mtg	Methiozolin RD Briefing	
EFED Neonic Biweekly		
EFED Neonic Biweekly		
EPA SFIREG Dicamba Ad hoc Workgroup		

All	Modeling
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Monday	Tuesday
Pyraziflumid: New Active Ingredient- Pre-submission meeting Chlorpyrifos Bi-Weekly	Pesticide Usage meeting w/Services
OPP Weekly Staff Mtg	EFED/BEAD General
	Difenoconazole DRA kick-off
NF-180: Presubmission Meeting	
	Reduced Risk Voting for Flutianil
- Atrazine (Triazine) Monitoring Program/Label Restrictions Discussion with PRD - Chlorpyrifos Biweekly OD Update	
SYN549522: Presubmission Meeting for Reduced Risk Questions	
	Pre-Subm for New Fungicide - Nisso Reduced Risk Voting-Flutanol
	Pollinator Webinar- Jon Zawislak - Pollen foraging by honey bees in agricultural landscapes
	Pyrethroids - Mitigation Biweekly with PRD

5/10/2019		
Wednesday	Thursday	Friday
DC Cir. Pests. Weekly Call		
Placeholder Synergy Briefing pre-meet		
RD/EFED General	EFED/AD General	
Meet with Arctic Slope Mission Services (ASRC) Contract Team to Discuss OPP's Public Docket Comments Task Order - 929		
Neonic off-week EFED meeting	-Neonic biweekly meeting w/ PRD -Cyantraniliprole S3NU 1st team mtg	
	Flutianil First Team Meeting	
	ESA Team Lead	
- Chlorpyrifos: Biweekly Team Meeting - Pyrimethanil: PRD Kickoff Meeting for RR	Dinotefuran (Neonics) Biweekly PRD Meeting	
OPPEL Coordination Team Meeting		
	Bayer - Spiromesifen	
Permethrin Check in with RD Permethrin PBPK Updates with PRD	MCPB - DRA explanation with PRD Spirotetramat - Reg Review Round 2 with PRD	

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	Phloxine B - New AI Pre-submsiion Meeting
Pyraziflumid: New Active Ingredient- Pre-submission meeting Rodenticide DRA	
GeoPlatform	
	ESA Weekly Check-in
	PWC Scenarios update

2019 Dicamba Information		
GIS Team - Qlik Demo		
Environmental Modeling Community of Practice	SAM Weekly Check-in	
Methomyl/Carbaryl Team Meeting		

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Monday	Tuesday
Drinking Water Follow-up at Hdqrs	Pesticide Usage Mtg w/Services Atrazine Eco Risk Assessment Pesticide Usage Mtg w/Services
OPP Weekly Staff Meeting	EFED General w/Rick
Monthly chemical Review	
	Sabadilla alkaloids meeting w/ MGK
	Dikegulac Pollinator DRA Preview with PRD Tembotrione DRA Kick-off Meeting
	Atrazine: AA Eco Risk Assessment Briefing
	Pyridaban Mitigation Prothioconazole Pre-submission Mtg
	Ethoprop Team Meeting with PRD
	Sulfoxaflor Colony Feeding Study Meeting with Dow and Smithers

5/3/2019		
Wednesday	Thursday	Friday
Placeholder Synergy Briefing pre-meet	Senior Science Advisor/Manager Forum	
	Discussion with Bayer re Non-target arthropod data Discusswion w/Corteva	
EFED/ITRMD General HED/EFED Monthly	Resources Meeting	
	Oxyfluorfen DRA briefing for PRD	
Neonic biweekly EFED meeting	Indoor fumigant meeting w/ PRD	
	ESA Team Lead Meeting	
Neonics: Biweekly Team Meeting	- Penoxsulam 1st Team Meeting - Atrazine Monitoring Data Discussion with PRD	
OPPEL Team Meeting	ESA Team Leader Meeting	
Rotenone Acrolein Team Mtg Methomyl/Carbaryl Team Mtg		
EFED Neonic Biweekly Meeting	Fumigant check-in w PRD Oxadiazon - DRA meeting w PRD	

ERB6	Other
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All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)

	Chlorine dioxide data requirements w/ RD
EPA GIS Workgroup Meeting	

EFED Neonic Biweekly	Phenothrin Enriched Isomer 1st Team Mtg w/ RD	
SFIREG EPA Dicamba Adhoc Workgroup		

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		Other

Monday	Tuesday
	Pesticide Usage Mtg w/Services
	EDSP Meeting at Hdqrs
OPP Weekly Staff Meeting RD/EFED General	
	Pesticide Usage Meeting w/Services
	Propargite DRA PRD briefing
	Metconazole DRA kick-off 2,4-D choline 24(c) meeting
	Sabadilla alkaloids meeting w/ MGK
	RD/EFED Tetraniliprole Follow-Up Pyrethroids Eco Mitigation
- Chlorpyrifos: OD Biweekly Update - Triazine: HH Risk Mitigation with PRD	
	Pyrethroids Ecological Mitigation with PRD

4/26/2019		
Thursday		Friday
Placeholder Synergy Briefing Pre-meeting	Systematic Review in Exposure Science Summit	
	2019 Dicamba Cals w/AAPCO	
RD/EFED General	EFED/BEAD General	
	EARTH DAY-Four Mile Run Stream Cleanup	
Difenoconazole DRA kick-off Neonic EFED off-week meeting	Indoor fumigant DRA kick-off Thiamethoxam PRIA & PID meeting Neonic biweekly meeting w/ PRD	
Mandipropamid Pre-Docket Opening Meeting	Paraquat DRA Risk Conclusions Starlicide PID Team Meeting	
	ESA Team Lead	
- Atrazine: PRD Pre-briefing for AA - Chlorpyrifos: Biweekly Team Meeting - Pyrimethanil: RR 1st Team Meeting	Neonics: Biweekly with PRD	
	Halauxifen: Corteva Meeting	
	- ESA Team Leaders - SmartLabel Use Index Workgroup	
Afidopyropen First Team Mtg		
	EFED Pollinator Team hosts Webinar by Dr. Harmon-Threatt - Neonicotinoid drift and contamination	
EFED Neonic Off-week Biweekly	Neonic Biweekly w/ PRD Structrual Fumigants DRA Kickoff w/PRD	

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Section 18 Potassium Chloride-zebra mussels Comments	
EPA GIS Workgroup Meeting	EPA GIS Workgroup Meeting

EFED Neonic Off-week Biweekly	Neonic Biweekly w/ PRD	
	ESA Species Weekly	
	SAM weekly	

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Comment: U.S. EPA User or Contractor:
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Monday	Tuesday
National Honor Awards -WJCE	AAAs Fellows interview
	Pesticide Usage Mtg w/Services
Chlorpyrifos Bi-Weekly	
EFED/BEAD General	
Full SFIREG Meeting	Placeholder Synergy Briefing pre-meet
Zoxamide PID meeting	
	Pyrethroids Mitigation
Chlorpyrifos OD Biweekly Meeting	
Dinotefuran RR Mitigation Mtg w/ Mitsui	
	Pyridaben Mitigation PRD-EFED
AQ (9,10-Anthroquinone)-Arkion/Landis	
NAPPC Pesticide Education Task Force Mtg	
	Saflufenacil - RR Round 2 with PRD Pyrethroids Mitigation

4/12/19		
Wednesday	Thursday	Friday
Executive Briefing on OPP Workflow Salesforce	Syngenta Presents-New Active Ingredient:Development and Decision Process	
DD Briefing: Atrazine	ESA/Pesticide Sr. Mgrs w/Services	
	EFED/AD General	
	OCSPP First Line Supervisors Forum Monthly	
Neonics EFED off-week meeting	GnRH RR Round 2 1st team meeting Neonics biweekly meeting w/ PRD	
	Methomyl/Thiodicarb Risk Management	
	ESA Team Leads	
- Atrazine DD Briefing RR Path Forward - Chlorpyrifos Biweekly Team Meeting	Methomyl (and Thiodicarb): PRD Risk Management Meeting	
	- ESA Team Leads - SmartLabel Index Workgroup	
	Carboxin DRA Briefing Pyroxsulam RR round 2 first team mtg	
EFED Neonics Off Week	Neonic Bi-weekly with PRD Sodium Cyanide Public Comments with PRD	

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	WoE Weekly

EFED Neonic Teams Biweekly Tebuconazole RR Team Mtg	Neonic Biweekly w/ PRD & BEAD Picarbutrazox New a.i. ROCKS Mtg	
Bulletins Live Two Webinar		
BLT Webinar	ESA Team Leads	
	Scenarios Check-in, SAM Weekly	
EISB Branch Meeting		

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Wednesday	Thursday
	Senior Science Advisor Managers Forum
Chlorothalonil Briefing w/DDs	Atrazine pre-briefing ESA/Pesticide Sr. Mgrs Mtg
HED/EFED General EFED/ITRMD General EFED General w/Rick	Resources Meeting PRD/EFED General
	Major Changes to USGS Water Quality Monitoring
Thiamethoxam meeting w/ Syngenta	
-Neonic biweekly EFED meeting -Broflanilide NC ROCs meeting w/ HED	-Non-field fumigants coordination -Dithiopyr PID planning meeting
	ESA Team Leads
	CLA/RISE
EFED Neonic Bi-weekly	Formetanate HCL - Meeting with PRD
Bayer/NuFarm Mitigation Discussions for Imidacloprid	
Cyanamide NU w/ RD EFED Neonic Biweekly	

4/5/19

Friday

Iprodione water modeling
Honey bee colony model sim

CLA/RISE

EISB	Registrant
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All	
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Clothianidin RR Mitigation Mtg w/ Valent & MGK	
GeoPlatform Monthly	EZ Tech Meeting
	FY18 ESA Expenditures Briefing, ESA WoE Weekly
	Managing EFED Models Team Meeting

SFIREG EPA Dicamba Ad hoc Workgroup	
BLT Development Workgroup	ESA Team Leads
	SAM Check-in
EISB Branch Meeting	

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ERB3	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
	Other
ERB4	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
	Other
ERB5	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
	Other
ERB6	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)

Monday	Tuesday
Clorpyrifos Bi-Weekly	Updated invitation: Pesticide Usage Meeting W/Services
OPP Weekly Staff Meeting	PRD/EFED General
NMFS meeting to discuss public comments on 2017 BiOp	CBD vs EPA Mtg
	Fluazifop Discussion
Chlorpyrifos: OD Biweekly Update	
	DOW:Aminopyralid, Picloram, Triclopyr and Clopyralid
	EPA/PMRA Joint Chemicals
	Aminopyralid, Picloram, Triclopyr and Clopyralid w/ Dow and PRD
Structural Fumigant OD Briefing	

3/29/19		
Wednesday	Thursday	Friday
	HOLD for Mefentrifluconazole D.D. Briefing	
Chlorpyrifos Bi-Weekly	Registration Review w/Keigwin ESA Team Mtg	
EFED/BEAD General EFED/FEAD General		
	Registration Review: Data Delays and Options w/Keigwin	
Environmental Modeling Public Meeting		
Neonic EFED off-week meeting	Neonic biweekly meeting w/ PRD	
Tetraniliprole Follow-up		
Chlorpyrifos: Biweekly PRD Meeting	Neonics: PRD Biweekly	
EMPM	SmartLabel Use Index	
Ametryn Comments		
	EFED Social EFED Pollinator Team Webinar - Samuel Ramsey: Varroa destructor	
EMPM		
EFED Neonic off-week Biweekly	Mefentrifluconazole: New Chemical briefing for DDs Neonic Biweekly with PRD	
EFED Neonic off-week Biweekly	Neonic Biweekly w/ PRD	

EISB	Registrant
	IT
	ESA
	Modeling
	Other
All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)

	- Picloram, Aminopyralid, Triclopyr, & Clopyralid w/ Dow & PRD - Aminocyclopyrachlor w/ Bayer & RD

	Pyrethroid Working Group Demonstration	
Step 2 Usage Meeting	ESA Team Leads	
	Scenarios check-in, SAM Weekly	

WEEK AT-A-GLANCE (WAAG)		
IO	BRANCH	
		Stakeholder/Briefing
		Risk Assessment
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
		Other
	ERB1	Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB2	Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB3	Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB4	Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB5	Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant

Monday	Tuesday
	Pesticide Usage Mtg w/Services
ESA Case Mtg w/Director	ESA Response re Comments on Revised Methods CBD vs EPA Settlement Issues
OPP Weekly Staff Meeting	ITRMD/EFED General
Consolidated Case Mtg w/Director	Regular monthly check-in with EFED and ITRMD on ESA Knowledgebase
Meeting w/ American Phytopathological Society representative	
	Non-field fumigants DRA EFED meeting
	Dikegulac-sodium joint PID/DRA discussion with PRD
Chlorothalonil: PRD DD Briefing Run-through	
	EFED COR Meeting with CDM-CSS
	TPTH DWA meeting with PRD
	USGS Ammonia
	OPP Recruitment Pollinator Team Biweekly
	Non-field fumigants DRA EFED meeting Cyazofamid: IR-4 New use meeting with RD

3/22/19		
Wednesday	Thursday	Friday
	Monthly Chemical Review	
	ESA/Pesticide Sr. Mgrs Meeting	
Tetranilipole Discussion w/Bayer Prep for Mtg w/NMFS		
EFED General w/OPP Director ITRMD/EFED General		
Resources Meeting	Senior Science Advisor Manager Forum	
-Captan PID meeting -Neonic biweekly EFED meeting		
Fluazifop-p-butyl use discussion with BEAD		
Tetraniliprole discussion with Bayer		
	ESA Team Lead	
Neonics: Biweekly EFED Meeting		
	SmartLabel Use Index	
TPTH Registration Review Team Mtg for PID		
	Varroa mite Control - essential oil	
EFED Neonic Biweekly	WDBjr monthly Chapter Mtg	
Neonics: Biweekly EFED Meeting Mefentrifluconazole: RD DD Briefing Run-through	Pyraflufen-ethyl: New use meeting RD	

ERB6	Other
	Stakeholder/Briefing
	Risk Assessment (RA)/ Problem Formulation (PF)
	Registrant
EISB	
	IT
	ESA
	Modeling
	Other
All	
	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)

	EFED Models Team
	EPA Geospatial Advisory Committee, Documents Team

EFED Neonic Biweekly		
SFIREG EPA Ad hoc Dicamba Workgroup		
	Usage Check-in, ESA Team Leads	
	SAM Weekly	
EISB Branch Meeting		

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday
IO		Stakeholder/Briefing
		Non-field fumigants DRA w/ERB!
		Risk Assessment
		Path Forward w/Pet Incidenta w/OPP Director Mtg re Consolidated ESA Case w/Director
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
		Other
		OPP Weekly Staff Meeting ECM Index Options w/ERB1
ERB1		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
ERB2		
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
ERB3		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
ERB4		Registrant
		Other
		Chlorpyrifos: OD Biweekly Update
ERB5		
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other

Tuesday	Wednesday
	EFED ALL HANDS MTG
Pesticide Usage Mts w/Services	Placeholder: ESA response to comments/updated methods description document
Placeholder: ESA response to comments/updated methods description document	
ORD/EFED General	
CBD Vs. EPA	PRIA Quarterly Stakeholder Mtg
	-Sabadilla alkaloids DCI discussion -Neonic EFED off-week meeting
Pyrethroids Eco Mitigation with PRD	
Tau-fluvalinate: RD Meeting New Uses	Chlorpyrifos: Biweekly Team Meeting
P-Dichlorobenzene (PDCB) and Napthalene PID team meeting	

3/15/19	
Thursday	Friday
Insecticide Application Methods Presentation by the Entomological Society of America Liaison, Allan Felsot	
More Discussion of EFED's Preliminary Protocol Reviews with Registrants	
EFED and Ent Soc Liaison	
Meeting with Entomological Society of America liaison Allan Felsot	
-Chlorfenapyr S3NU kick-off meeting	
-Neonic biweekly meeting w/ PRD	
Florchlorfenuron DRA Kick-off	
ESA Team Lead	
Neonics: Biweekly PRD Meeting	
SmartLabel Use Index	
Insecticide Application Methods Presentation by the Entomological Society of America Liaison, Allan Felsot	

	ERB6	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
		Stakeholder/Briefing	
	EISB	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		IT	
		ESA	
		Modeling	
		Other	
	All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)	

Pyrethroids Eco Mitigation with PRD	
	EFED: Non-field fumigant planning
	EFED Biweekly Neonic Mtg
	SFIREG EPA Dicamba Ad Hoc Workgroup
	BLT Dicamba Post-Mortem

NAA (Naphthaleneacetic Acid and Salts) DRA Meeting with PRD	
Neonic Biweekly w/ PRD & BEAD	
ESA Team Leads	
SAM Weekly, Scenarios check-in	
GIS Team meeting	

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday
IO		Stakeholder/Briefing
		Synergy Meeting with Industry - EPA Confirmed
		Risk Assessment
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
		OPP Weekly Staff Meeting
	ERB1	Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Novaluron DRA kick-off
	ERB2	Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
	ERB3	Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
	ERB4	Registrant
		Other
		Synergy Meeting with Industry
		Stakeholder/Briefing
	ERB5	Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
		Stakeholder/Briefing

Tuesday		Wednesday	
California AG Commissioners Mtg			
Non-field fumigants DRA Pesticide Usage Meeting w/Services ESA Mtg at Hdqrts		ESA Pesticide Mtg w/Services	
ITRMD/EFED General		HED/EFED General Resources Mtg	
Discussion w Croplife Board of Directors			
Non-field fumigants DRA EFED meeting		Neonic EFED biweekly meeting	
Triademifon DCI follow-up with PRD			
Usage Workgroup			
		Neonics: EFED Biweekly Meeting	
Pethoxamid Use Maximum Use Rate		L-Glufosinate and data comp	
Non-Field Use Maximum Use Rate		Neonic EFED Bi-weekly Mtg	

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<div>ERB6</div> <div>EISB</div> <div>All</div>	Stakeholder/Briefing	
	Risk Assessment (RA)/ Problem Formulation (PF)	Mesotrione RR Team Mtg Initial Rodenticide Mtg w/ PRD
	Registrant	
	IT	
	ESA	BLT Presentation @ AAPCO
	Modeling	
	Other	GeoPlatform Monthly
	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)	

	EFED Neonics Biweekly
EZ Tech Meeting	
Scenarios Check-in	
	EISB Branch Meeting, GIS Workgroup Monthly

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday
IO		Stakeholder/Briefing
		Risk Assessment
		2,4-D Discussion with APVMA and NSW EPA Chlorpyrifos Bi-weekly
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
	ERB1	OPP Weekly Staff Meeting
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Hydramethylnon RTC OPP meeting
	ERB2	Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
	ERB3	Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Chlorpyrifos Biweekly OD Update
	ERB4	Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
	ERB5	Registrant
		Other
		Methiozolin DW Assessment
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)

Tuesday	Wednesday
	EFED New Employee Training
Pesticide Usage Meeting with the Services	SRAC biweekly meeting
Dicamba+S-Metolachlor Premix Discussion with Syngenta.	
EDSP Science and Policy Committee	
EFED/PRD General	FEAD/EFED General BEAD/EFED General
CBD Call	ERB#'s Social Hour +
	Novaluron DRA kick-off Neonic EFED off-week meeting
Triademifon DCI follow-up with PRD	
Usage Workgroup	
	EFED Neonics Biweekly Meeting
	P-Dichlorobenzene (PDCB) PID team meeting
	RD - New Chemical Briefing - Metentrifluconazole
	EFED Neonic Biweekly

	3/1/19
Thursday	Friday
Senior Science Advisor-Managers Forum Bi-Weekly Meeting	
ESA/Pesticide Sr. Mgrs Call Metribuzin Team Meeting (Rescheduled)	
ESA Team Meeting - getting back on calendars	
Tetraconazole DRA kick-off Neonic biweekly meeting w/ PRD	
Tetraniliprol pre-meet conference call with Bayer	
ESA Team Leads	
Neonics Biweekly with PRD	
Flonicamid: ISK Discussion on Higher Tier Studies for RR	
SmartLabel Use Index Group	

ERB6	Registrant	
	Other	
	Stakeholder/Briefing	
	Risk Assessment (RA)/ Problem Formulation (PF)	Ethaboxam NU Check-in w/ RD
	Registrant	
	IT	
	ESA	
	Modeling	
	Other	
EISB		
All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)	

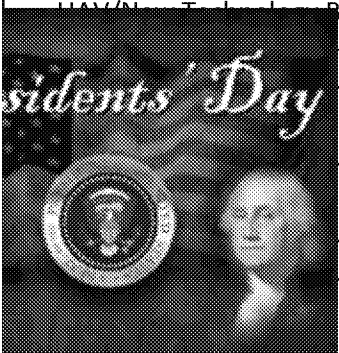
Aliphatic Solvents Mitigation w/ PRD Chlorflurenol RR Team Mtg w/ PRD	EFED Neonics Biweekly
Dicamba+S-metolachlor w/ RD & Syngenta	
	SFIREG EPA Dicamba Ad Hoc Workgroup
Usage Workgroup	BLT SFIREG Webinar
SAM Check-in	
	EISB Branch Meeting

Neonic Biweekly with PRD Picarbutrazox NC Team Mtg Metribuzin RR Team Mtg	
CETIS core group updates	
ESA Team Leads	
SAM Weekly, Scenarios check-in	

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday
IO		Stakeholder/Briefing
		Risk Assessment
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
		Other
	ERB1	
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB2	
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB3	
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB4	
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB5	
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
	ERB6	
		Stakeholder/Briefing



Tuesday		Wednesday	
	Pre-briefing Hqrs	Pre-brief OPP discussion on the response to the Draft OIG Report on Pesticide Registrations	
	Pesticide Usage line		
	Issues		
		ITRMD/EFED General EFED General with OPP	
CBD v. EPA		EFED New Employee Training	
		Neonic EFED biweekly meeting	
Napropamide DRA First Team Meeting			
Thiabendazole: DRA Check-in with PRD		Neonics Biweekly EFED Meeting	
		EFED biweekly meeting	

2/22/19	
Thursday	Friday
New Chemical Briefing for EFED Director- Metentriflu Conazole	
Discuss EFED's Preliminary Protocol Reviews with Registrants	
Prohexadione-Ca 90-d screen meeting	
Triadimefon meeting	
Triticonazole: DRA Kickoff with PRD	
- ESA Team Lead Meeting - SmartLabel Use Index Workshop	
Acetamiprid Team Meeting	
DD - New Chemical Briefing - Metentrifluconazole	

EISB	Risk Assessment (RA)/ Problem Formulation (PF)	
	Registrant	
	IT	
	ESA	
	Modeling	
	Other	
All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)	

Chlorine Dioxide New AI w/ RD & AD	EFED Neonics Biweekly
	SFIREG EPA Dicamba Adhoc Work Group
EPA Usage Workgroup, Probabilistic Method Development, ESA Tool QC PWC Post-Processor	CEQ/Services/USDA Revised ESA Methods Meeting
DD Scenarios Meeting, SAM Check-in	
EPA Geospatial Advisory Committee, Documents Team Meeting	EISB Branch Meeting

- Picarbutrazox New AI w/ RD & PMRA - ERB6 Regroup on Dicamba DGA + S- metolachlor Premix	
ESA Leads Meeting	
SAM Weekly	

WEEK AT-A-GLANCE (WAAG)

IO	BRANCH	Monday	
		Stakeholder/Briefing	EFED Planning
		Risk Assessment	
		Registrant/Applicant/Tour	
		SAP/CRP/EDSP	
		Other OPP & Div. Meetings	OPP Weekly Staff Meeting
		Other	
	ERB1	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB2	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB3	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	Chlorpyrifos: Biweekly OD Update
		Registrant	
		Other	
	ERB4	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB5	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB6	Stakeholder/Briefing	

Tuesday	Wednesday
	USMCA-IWG Meeting
Pesticide Usage Mtg	
PRD/EFED General	FEAD/EFED General
EFED Planning	EFED New Employee Training
Hydramethylnon RTC OPP team mtg	Neonic off-week EFED meeting
New Chemical (XDE-659) briefing from registrant	Syngenta presentation on conservation program (ESA)
-Inter-Agency Pesticide Usage Meeting	EFED New Employee Training
Flutriafol: NOF Comment Discussion with RD	EFED Neonics Biweekly Meeting
	Acetamiprid: Mitigation and PID Team Meeting
	Placeholder - Syngenta presentation on conservation program

2/15/19	
Thursday	Friday
NDGGA: Planning for 2019 Crop Tour ESA/Pesticide Senior Managers w/Services	
EFED/ITRMD General	
Atrazine: Risk Management Options PRD Meeting	
SmartLabel Use Index Workshop	
L-Glufosinate Pre submission meeting with Landis International, Inc	

EISB	Risk Assessment (RA)/ Problem Formulation (PF)	
	Registrant	
	IT	
	ESA	
	Modeling	
	Other	
All	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)	

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday	Tuesday
IO		Stakeholder/Briefing	
		Risk Assessment	
		Registrant/Applicant/Tour	
		SAP/CRP/EDSP	
		Other OPP & Div. Meetings	
		Other	
	ERB1		
		Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
	ERB2	Other	
		Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
	ERB3	Registrant	
		Other	
		Stakeholder/Briefing	
	ERB4	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB5	Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
		Other	
	ERB6		
		Stakeholder/Briefing	
		Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant	
	EISB		
		IT	
		ESA	

[illegible]

All	Modeling		
	Other		
	Entries for "OPP Weekly Report" (Branch/Subject/Presenter)		

WEEK AT-A-GLANCE (WAAG)

BRANCH		Monday
IO		Stakeholder/Briefing
		Leadership Budget Briefing
		Risk Assessment
		Registrant/Applicant/Tour
		SAP/CRP/EDSP
		Other OPP & Div. Meetings
		Other
ERB1		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
ERB2		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
ERB3		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
ERB4		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
ERB5		Stakeholder/Briefing

Tuesday	Wednesday
ESA strategy and next steps briefing for DDs	Update on OECD Pollinators Project
Dicamba analysis - - information sources Neonic Risk Assessments Dicamba Briefing Pesticide Usage Meeting w/the Services	Dicamba w/Nancy Beck Consolidated ESA Cases w/Rick
External Meeting - Paradigm Convergence Technologies Inc.	
EDSP Science & Policy Committee	
	Resources Meeting
	Best in Science - action plan Update on OECD Pollinators Project
	-Linuron PID meeting -Neonic biweekly EFED meeting
	Carbaryl/Methomyl Team Meeting
	Inter-Agency Mosquito Adulticide Usage Group
	- Neonics Biweekly Team Meeting - Valifenalate TOXSAC
	Diphenylamine RR PID

7/27/18

Thursday	Friday
Pre-brief: Overview of OPP's Grants Senior Science Advisor - Management Forum Follow up on DD Briefing on Seed/Granular Incorporation	
ESA/pesticide Sr. Managers	
Check in on EDSP Activities	
EFED General w/Rick Keigwin	
BASF Mallard Reproduction Study Discussion	
SmartLabel Use Index Workgroup	

ERB6	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
		IT
		ESA
		Modeling
		Other
		Entries for "OPP Weekly Report" (Branch/Subject/Presenter)
EISB	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
		IT
		ESA
		Modeling
		Other
		Entries for "OPP Weekly Report" (Branch/Subject/Presenter)
All	Risk Assessment (RA)/ Problem Formulation (PF)	
		Registrant
		Other
		Stakeholder/Briefing
		Risk Assessment (RA)/ Problem Formulation (PF)
		Registrant
		Other
		IT
		ESA
		Modeling
		Other
		Entries for "OPP Weekly Report" (Branch/Subject/Presenter)

Triclopyr: PRA Kick-Off Meeting	- EFED Neonic Biweekly
Methiocarb RR Mtg w/ PRD, tent. Mesotrione GMO New Use w/ RD	Neonic Residue Strategy Team Mtg
	IA Mosquito Usage Group
SAM Check-in	BEAD feedback on EFED scenarios
EFED Ice Cream Social	EISB Branch Meeting

ESA Team Leads	
SAM Weekly	

Message

From: Lin, James [lin.james@epa.gov]
Sent: 9/26/2019 3:55:00 PM
To: Corbin, Mark [Corbin.Mark@epa.gov]; Blankinship, Amy [Blankinship.Amy@epa.gov]
CC: Went, Stephen [Wente.Stephen@epa.gov]
Subject: RE: NMC Cumulative Risk Assessment (CRA)

Mark:

Thanks much for forwarding the report.

Based on the summaries of NMC CRA below, the current approach in the methomyl DWA is consistent with the NMC report.

Please advise if any comments.

Thanks much.

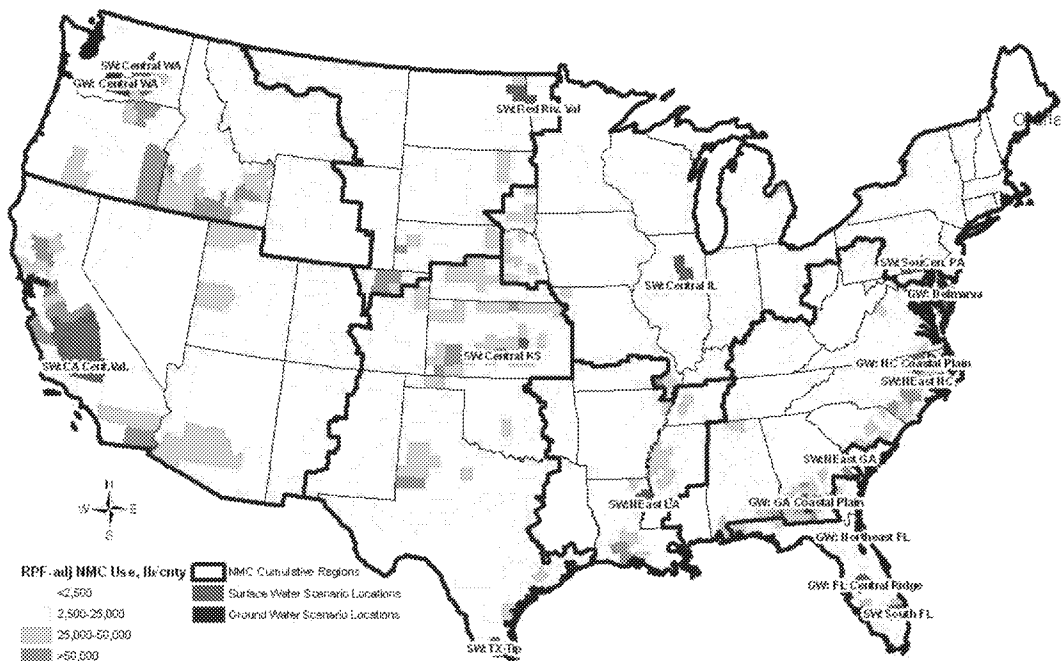
Jim

OPP selected Locations where NMC residues in drinking water sources are likely to be of greatest concern based on:

- **Relatively high NMC use:** both total NMC use by county and relative potency-adjusted NMC use were considered; for ground water sources, EPA also looked at the areas with the highest aldicarb and carbofuran uses;
- **Nature and source of drinking water:** EPA used the USGS report on water use in the U.S. (USGS, 1998, 1999) to identify the drinking water sources (public surface water, public ground water, domestic private) by county and information on surface water intake locations to identify the dominant drinking water sources in high NMC use counties;
- **Vulnerability of the drinking water sources:** vulnerability of surface water sources was based on the relative runoff potential of the watershed area around surface water intakes; vulnerability of ground water sources was based on the leaching potential of the overlying soils and vadose zone.

There are six groundwater modeling scenarios developed as identified in Figure 1 (from the NMC report). Among these, only the west coast one (Central WA) is not used in our current PWC-GW scenarios. The PWC-GW scenarios including: Delmarva-sweet corn, FL-potato, FL-citrus, GA-peanuts, NC-cotton, and WI-corn. Based on the methomyl use information, the use of two FL scenarios is appropriate. If addition scenario is to be considered, Delmarva-sweet corn should be added.

Figure 1. NMC CRA regions for drinking water exposure assessment showing high NMC use areas and regional drinking water exposure sites



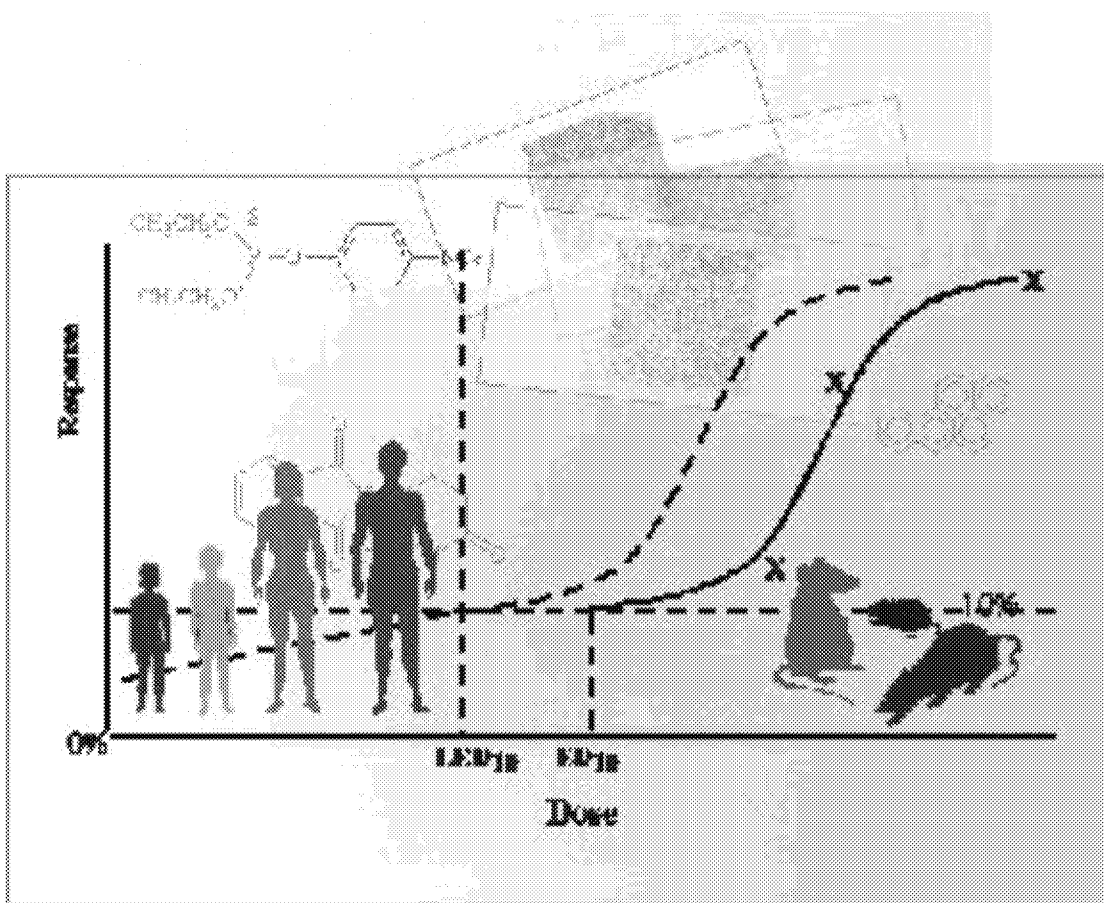
From: Corbin, Mark <Corbin.Mark@epa.gov>
Sent: Tuesday, September 24, 2019 2:54 PM
To: Blankinship, Amy <Blankinship.Amy@epa.gov>
Cc: Wente, Stephen <Wente.Stephen@epa.gov>; Lin, James <lin.james@epa.gov>
Subject: NMC Cumulative Risk Assessment (CRA)

Pdf and Word versions. You will see in here that as with the OP's the focus for the assessments was on regions of high use.

Mark Corbin
Branch Chief, Environmental Risk Branch 6
Environmental Fate and Effects Division (7507P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington DC 20460
703-605-0033



Revised *N*-Methyl Carbamate Cumulative Risk Assessment



U.S. Environmental Protection Agency
Office of Pesticide Programs
September 24, 2007



Revised *N*-Methyl Carbamate Cumulative Risk Assessment

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Technical Executive Summary

With the passage of the FQPA (1996), EPA was required to consider available information concerning the cumulative effects on human health resulting from exposure to multiple chemicals that have a common mechanism of toxicity. In 2001, the Agency identified the *N*-methyl carbamate (NMC) pesticides as a group which shares a common mechanism and published a preliminary Cumulative Risk Assessment (CRA) in 2005. A cumulative risk assessment incorporates exposures from multiple pathways (i.e., food, drinking water, and residential/non-occupational exposure to pesticides in air, or on soil, grass, and indoor surfaces) for those chemicals with a common mechanism of toxicity.

Since the release of the preliminary NMC CRA, the Agency has incorporated new hazard and exposure data, assigned FQPA safety factors, evaluated comments from the public, and addressed comments by the FIFRA Scientific Advisory Panel (SAP). In addition, since 2005, the Agency's Office of Pesticide Programs (OPP) has completed several additional risk assessments for individual NMC pesticides (aldicarb, carbaryl, carbofuran, methomyl and propoxur) and, where necessary, established mitigation measures to be implemented to reduce exposure to these pesticides. These mitigation measures are reflected in this revised NMC CRA.

The methodology used in this revised CRA is similar to that used in the preliminary CRA and supported by the SAP (USEPA, 2005a,b). Throughout the development of this CRA, EPA has relied on the SAP to peer-review guidance documents, methods, approaches, and pilot analyses to ensure that appropriate methods and sound science were applied. In addition to the SAP reviews, EPA has sought and considered public comments on these approaches as it developed these cumulative assessment methods.

Background:

A CRA begins with the identification of a group of chemicals, called a Common Mechanism Group (CMG), which induces a common toxic effect by a common mechanism of toxicity. Pesticides are determined to have a "common mechanism of toxicity" if they act the same way in the body--that is, the same toxic effect occurs in the same organ or tissue by essentially the same sequence of major biochemical events. The NMCs were established as a CMG by EPA in 2001 (USEPA, 2001a) based on the shared structural characteristics and similarities and their shared ability to inhibit acetylcholinesterase (AChE) by carbamylation of the serine hydroxyl group located in the active site of the enzyme. When AChE is inhibited, acetylcholine accumulates and cholinergic toxicity results due to continuous stimulation of cholinergic receptors throughout the central and peripheral nervous systems that innervate virtually every



organ in the body. An important aspect of NMC toxicity is the rapid nature of the onset and recovery of effects; following maximal inhibition of cholinesterase (typically between 15 and 45 minutes), recovery occurs rapidly (minutes to hours).

Once a CMG is identified, it is important to determine which chemicals from that group should be included in the quantification of cumulative risk. The group of pesticides which is included in the quantification of cumulative risk -- and consequently incorporated into the CRA -- is termed the Cumulative Assessment Group (CAG). In determining the specific NMC pesticides to be included in the CAG, EPA considered risk mitigation decisions and exposure potential. EPA identified three exposure pathways of interest for these pesticides: food, drinking water, and residential/non-occupational. Each of these pathways was initially evaluated separately, and -- in performing this portion of the analysis -- EPA determined which of the NMCs were appropriate to include for each given pathway. The cumulative assessment of potential exposure to NMCs in food includes those which are currently registered in the U.S. or have import tolerances. The drinking water exposure pathway includes NMC pesticides with registered uses in the U.S. that can potentially reach water bodies or ground water (i.e., outdoor uses). The revised NMC CRA evaluates the residential exposure pathway for three pesticides registered in the U.S. (carbaryl, methiocarb and propoxur) for home use. The current assessment reflects the most up-to-date and best available information for these chemicals.

There are many steps involved in quantitatively assessing the potential human health risk associated with exposure to the NMC pesticides. The complex series of evaluations involve hazard and dose-response analyses; assessments of food, drinking water, residential/non-occupational exposures; combining exposures to produce a cumulative risk estimate; and risk characterization. These steps are described more fully in OPP's Cumulative Guidance (USEPA, 2002a). The approach to each of these components and their results is briefly explained below:

- ☐ Selection of an index chemical to use as the point of reference to standardize the toxic potencies of each NMC, determination of the relative toxic contribution of each NMC, and establishment of a value to estimate potential risk for the group (i.e. point of departure);
- ☐ Evaluation of inter-species differences (i.e., extrapolation of rat responses to human responses) intra-species variability; and the potential sensitivity to infants and children;
- ☐ Estimation of the risks associated with all pertinent pathways of exposure (i.e., food, drinking water, residential) in a manner that is both realistic and reflective of variability due to differences in location, time, and demographic characteristics of exposed groups;
- ☐ Identification of the significant contributors to risk; and



- ❑ Characterization of the confidence in the results and the uncertainties associated with the assessment.

Hazard and Dose-Response Assessment:

EPA used the relative potency factor (RPF) method to determine the combined risk associated with exposure to NMCs. Briefly, the RPF approach uses an index chemical as the point of reference for comparing the toxicity of the NMC pesticides. RPFs are calculated as the ratio of the toxic potency of a given chemical to that of the index chemical and are used to convert exposures of all chemicals in the group into exposure equivalents of the index chemical. Because of its high quality dose response data for all routes of exposure, as well as high quality time-to-recovery data, EPA selected oxamyl as the index chemical for standardizing the toxic potencies and calculating relative potency factors for each NMC pesticide.

Toxic potencies for the NMCs were determined using brain AChE inhibition measured at peak inhibition following gavage exposures in rats. Brain AChE inhibition is a direct measure of the mechanism of toxicity and thus does not have the uncertainty associated with using blood measurements of cholinesterase inhibition which serve as surrogates for cholinesterase inhibition in the peripheral nervous system. Furthermore, relative toxic potencies derived from brain data were shown in the preliminary assessment to be similar to those derived from red blood cell data but showed less variability, and thus less uncertainty, when comparing potency across the NMCs.

The Agency used an exponential dose-time-response model to develop benchmark dose estimates at a level estimated to result in 10% brain cholinesterase inhibition (i.e., a benchmark dose or BMD₁₀) to estimate relative potency. The Agency has also calculated the half-life to recovery for brain AChE inhibition. The Agency has used the lower confidence limit on the BMD₁₀ (i.e., BMDL₁₀) to develop points of departure (PoD) from the oral, dermal, and inhalation routes for oxamyl, the index chemical. A PoD is a point estimate on the index chemical's dose-response curve from which risks associated with the exposure levels anticipated in the human population are extrapolated. EPA compares estimated exposures with the route-specific PoD values to calculate Margins of Exposure (MOE) and to estimate potential risk to humans.

The Agency has used available comparative cholinesterase studies in juvenile (post-natal day 11 and/or 17) and adult rats to evaluate the FQPA 10X safety factor. These studies are available for six NMCs. For these NMCs, the Agency calculated the BMD₁₀ in pups and adults—the ratio of these benchmark doses provides the chemical-specific FQPA factor. For the remaining NMCs without comparative data, a 10X factor was applied. For the inter-species extrapolation factors, there are studies with human subjects with three NMCs (aldicarb, methomyl and oxamyl) that were determined by EPA, after considering the advice of the Human Studies Review Board, to be ethically and scientifically acceptable for use in this risk assessment. These studies were used to derive the chemical-specific inter-species extrapolation factor for these three chemicals. For the remaining NMCs, the standard 10X factor was assigned for inter-



species extrapolation. Since each NMC has been assigned its own inter-species and FQPA safety factors, the Agency has mathematically applied the value of these factors directly to the RPF for each NMC. In addition, the Agency has used the standard 10X factor for intra-species extrapolation for all the NMCs. Thus, to account for intra-species extrapolation, the target MOE for the revised NMC CRA is 10.

Exposure Assessment:

An important aspect of the exposure analyses is to develop exposure scenarios resulting from the uses for each NMC. Three key pathways of exposure to NMC pesticides -- food, drinking water, and residential and other non-occupational settings -- were included in this assessment. The factors EPA considered in the analysis of exposure by each of these three pathways included duration, frequency, and seasonality of exposure. Evaluation of chemical use profiles allows for the identification of exposure scenarios that may overlap, co-occur, or vary between chemicals, as well as for the identification of populations of concern.

All of the hazard data, exposure data, and exposure scenarios must be combined in a manner designed to produce reasonable and realistic estimates of exposures likely to be encountered by the public in location and time of year. As was done in previous CRAs, EPA used Calendex™ software to integrate various pathways while simultaneously incorporating the time dimensions of the data. Calendex™ provides a focused, detailed profile of potential exposures to individuals across a calendar year. LifeLine™ software was also used to evaluate exposures through the food pathway and these results are presented and discussed in Appendix C. Exposures through residential uses and in drinking water are incorporated into cumulative exposure assessments on a regional basis. EPA conducted regional assessments for drinking water and joined these with generic residential exposure scenarios generally representative of regions in the Southern U.S. These regional assessments reflect the highest potential exposure scenarios for the U.S. and account for differing agronomic uses and reflect the differences in climate, soil conditions, and pest pressures across the country. Exposures that are represented in these generic residential exposure scenarios are not expected to be exceeded in any region in the U.S. Exposure to NMC pesticide residues in foods is considered to be uniform across the nation (i.e., there are no significant differences in food exposure due to time of year or geographic location). The assumption of nationally uniform food exposure is based on the understanding that, to a large extent, food is distributed nationally and food consumption is independent of geographic region and season. The single national estimate of food exposure was combined with region-specific exposures from residential uses and drinking water in three regions that represent the highest potential for exposure.



Table ES -[SEQ Table * ARABIC \s 2]. Summary Information Regarding the NMC Pesticides and the Uses, and Pathways Included in the revised NMC Cumulative Risk Assessment

Pesticide	Pesticide Uses	Pesticide Pathways		
		Food	Drinking Water	Residential
Carbaryl	Ag Crops	X	X	
	Lawn			X
	Garden			X
	Ornamentals			X
	Fruit Trees			X
	Pet Collar			X
	Golfer Exposure			X
Aldicarb	Ag Crops	X	X	
Oxamyl	Ag Crops	X	X	
Formetanate HCl	Ag Crops	X	X	
Methomyl	Ag Crops	X	X	
Carbofuran	Ag Crops	X	X	
Propoxur	Food Uses	X		
	Pet Collars			X
Methiocarb	Ag Crops	X		
	Ornamental			X
Thiodicarb	Ag Crops	X	X	
Pirimicarb	Ag Crops	X		

The approach for each pathway of exposure and results for the revised NMC CRA are explained below:

Food:

The food component of the revised NMC CRA is considered to be highly refined and to provide reasonable estimates of the distribution of exposures across the U.S. The exposure estimates for food are based on residue monitoring data from the USDA's Pesticide Data Program (PDP) supplemented qualitatively with information from the Food and Drug Administration's (FDA) Pesticide Residue Monitoring Program and Total Diet Study. The PDP data provide a very reliable estimate of pesticide residues in the major children's foods and account -- directly or indirectly through the use of commodity surrogates -- for approximately 93% of food consumption by children. These data also provide direct measures of co-occurrence of NMC pesticides in the



same sample. PDP samples with non-detectable residues were treated in this assessment as "zero" values. Sensitivity analyses have determined that this approach does not significantly underestimate exposures at the upper percentiles for the NMCs (i.e., those percentiles which are of the greatest regulatory importance). For those foods not monitored in PDP, similar commodities that are measured by PDP served as surrogate data sources. This approach is considered to be reasonable and generally sound given that it is based on the concept that families of commodities with similar cultural practices and insect pests are likely to have similar pesticide use patterns and residue levels. Additionally, these surrogated commodities account for less than 1% of children's diets.

The reliability of the food component of this assessment is also supported by the use of the food consumption data from the USDA's Continuing Survey of Food Intakes by Individuals, (CSFII 1994-1996/1998). The CSFII surveyed more than 20,000 individuals over two non-consecutive days and provides a detailed representation of the food consumption patterns of the U.S. public across all age groups, during all times of the year, and across all 50 states. Thus, EPA has confidence that the consumption estimates for food are well-established and consequently support reasonable risk estimates for the U.S. population. The NMC CRA focuses on the following age groups: children 1-2 years old; children 3-5 years old; adults 20-49 years old; and adults 50+ years old. These age groups were selected since they provide a broad representation of potential exposures and because they include age groups that are commonly shown to be the most highly exposed in single-chemical assessments. Details regarding estimated exposures of other age groups are presented in the appendices to this report.

During the period since the issuance of the preliminary NMC CRA in August 2005, the Agency has further improved and refined its assessment of the cumulative risks associated with the NMC pesticides. These refinements include incorporating the most recent food residue data by including pesticide residue data through 2006 from USDA's PDP Program and updating the assessment to reflect individual risk mitigation measures and other use pattern changes for individual NMC pesticides. Specifically, during this period, the Agency has imposed risk reduction measures on some of the major contributors to carbamate cumulative risk. The risk estimates presented in the revised NMC CRA reflect the risk mitigation measures taken on individual carbamates since FQPA was signed into law in August 1996. In general, EPA's risk estimates contained in this CRA reflect mitigation measures that EPA determined to be warranted based on its assessment of the single chemical's risks. Since the preliminary assessment, the Agency has received a request for voluntary cancellation for methomyl on grapes and strawberries, has determined that carbofuran is ineligible for reregistration, and will implement certain label restrictions for aldicarb that will increase drinking water well set-backs in the southeastern coastal plains when certain criteria are triggered. Therefore, these uses (and exposures) are not included and the aldicarb label restrictions have been accounted for in the revised NMC CRA.

In evaluating exposure through the remaining uses on food, OPP concludes that a few uses of NMC pesticides on food crops generally play a larger role in contributing to



the cumulative risks of the NMC pesticides. These include use of aldicarb on potato; carbaryl on peach and strawberry; and methomyl on cantaloupe, watermelon, peach, spinach, and strawberry. However, evaluation of the total risk from exposure to NMCs in foods indicated that the cumulative MOEs from exposure to NMCs do not raise a concern. Specifically, the target MOE of 10 is reached at the 99.848th and 99.870th percentiles of exposure for the most highly exposed age groups, children 1-2 and children 3-5 years old, respectively. These percentiles are not considered meaningfully different from the 99.9th percentile. Associated MOEs range from 7.9 for the most exposed subgroup (children 1-2) to 42 for adults 20-49.

When developing any risk assessment, assumptions must be made in areas where data are not available. In the revised NMC CRA, the Agency has made health protective assumptions in its baseline analysis, particularly with regard to the years of PDP data which are used (for which it used all years of PDP data except in cases where use patterns have changed or will change), the use of a 10x inter-species extrapolation factor for those NMCs without human data, and summing exposures over a 24-hour period. In an effort to characterize and understand the MOEs estimated in this assessment, four sensitivity analyses were performed by the Agency to evaluate the degree to which key areas of the risk assessment may under- or over-estimate cumulative risk. The sensitivity analyses demonstrate that the Agency has not underestimated exposures through food and associated risks to any significant degree since these sensitivity analyses result in only small changes in the percentile at which the target MOE of 10 is reached. The results of the sensitivity analyses using the most recent PDP data and inter-species factors of 3x instead of the standard 10x for certain pesticides provide added certainty that risks are below the Agency's level of concern.

Residential:

Applications of NMC pesticides in and around homes, schools, offices, and other public areas may result in potential exposure via the oral (due to hand-to-mouth activity by children), dermal, and inhalation routes. There are three NMC pesticides with currently registered residential uses considered as part of the revised NMC CRA in the residential/non-occupational exposure pathway assessment. The residential uses considered in this assessment include the carbaryl uses on lawns, golf courses, fruit trees, and vegetable and ornamental gardens; the methiocarb snail and slug bait use; and the carbaryl and propoxur pet collar uses. In addition to the uses listed above, the preliminary NMC CRA also included an assessment of indoor spray uses of propoxur (crack and crevice). Since the preliminary assessment, the Agency has received a request for voluntary cancellation of all propoxur indoor spray uses that may result in non-occupational exposure for children. Therefore, these uses are not included in the revised NMC CRA.

Another notable change since issuance of the preliminary NMC CRA is the revision of the methodology used to assess children's hand-to-mouth exposure. The non-dietary ingestion pathway was the least refined of the residential exposure pathways modeled in the preliminary NMC CRA. The refined methodology used in this



revised assessment is based on recommendations from the August 2005 FIFRA SAP, and addresses limitations in the non-dietary oral pathway by modifying the probabilistic hand-to-mouth algorithm. This modified algorithm is a product of a collaborative effort between OPP scientists and the developers of the SHEDS (Stochastic Human Exposure and Dose Simulation) and CARES (Cumulative and Aggregate Exposure System) models.

For the residential/non-occupational exposure pathway, several reliable data sources were used to define how pesticides are used, how quickly the residues dissipate, how people may come into contact with pesticides (e.g., via dermal or inhalation exposure), and the length of time people might be exposed based on certain activities (e.g., playing on a treated lawn). As with the drinking water assessment (see below), the residential exposure assessment considers seasonal applications and timing as well as regional differences. In the case of regional differences, the revised NMC CRA considered the Southeast Region of the United States. Due to longer periods of pesticide use, this assessment provides a worst case estimate of exposure.

The results of the residential risk assessment indicate that remaining residential uses of NMCs -- as borne out by the analyses here -- are below OPP's level of concern for all subpopulations.

Drinking Water:

The drinking water assessment focuses on areas where combined NMC exposure is likely to be among the highest within each region as a result of total NMC usage and vulnerability of drinking water sources. This analysis is based on a probabilistic modeling approach that considers the full range of drinking water consumption and concentration data and not single high-end estimates. EPA estimated NMC exposures in drinking water to individuals in the CRA for both ground water and surface water sources of drinking water in each of three regions. The regional drinking water exposure assessments represent exposures from vulnerable drinking water sources resulting from typical NMC usage and reflect seasonal variations as well as regional variations in cropping and NMC pesticide use. Each regional assessment focuses on areas where combined NMC exposure is likely to be among the highest within the region as a result of total NMC usage, adjusted for relative potencies, and vulnerability of the drinking water sources. For ground water, private wells extending through highly permeable soil and vadose zone materials into shallow, acidic ground water are expected to be most vulnerable. For surface water, drinking water reservoirs in small, predominantly agricultural watersheds are likely to be most vulnerable. The co-occurrence of NMC residues in water is estimated primarily from modeling since sufficient monitoring data are not available to be the sole basis for the assessment. However, monitoring data are used to corroborate the modeling results and have helped confirm locations of potentially vulnerable drinking water sources.

In most of the country, NMC residues in drinking water sources are at levels that are not likely to contribute substantially to the multi-pathway cumulative exposure.



Estimated NMC exposures from surface water sources of drinking water resulted in MOEs well above 10. For most ground water sources of drinking water, NMC exposures were similarly low. Shallow private wells extending through highly permeable soils into shallow, acidic ground water represent what the Agency believes to be the most vulnerable drinking water sources for the NMCs based on available monitoring, current use patterns, and known soil and hydrologic conditions. Those instances where NMC concentrations resulted in MOEs of less than 10 are being addressed with mitigation measures in the single-chemical assessments – an increase in the well setback distance from 300 feet to 500 feet for aldicarb use on peanuts in the southern portion of the Coastal Plain and a notice of intent to cancel all domestic carbofuran uses. With these mitigation measures, NMC exposures from drinking water result in MOEs greater than 10.

Combined Pathway (Cumulative) Assessment:

EPA also evaluated total MOEs for all three pathways (food + water + residential) simultaneously. Evaluating exposures is significantly more complex when the analyses address the simultaneous exposures to more than one pesticide and when distributional inputs derived from data from surveys and monitoring studies – as opposed to default assumptions or point estimates – are used. The detailed multi-pathway graphical outputs presented in Part III of this report reflect individual and combined pathway MOEs at multiple percentiles of exposure over the course of an entire year and allow in-depth analysis of interactions of data sets to evaluate potential risk concerns and identify the sources of exposures. The graphical outputs improve the ability to interpret the complete risk picture. Based on the simultaneous evaluation of all three exposure pathways and their associated routes using the Calendex software, the MOEs at the 99.9th percentile are approximately 8 or greater for all populations. Generally, exposures through the food pathway dominate total MOEs, with residential exposures less throughout most of the year. Although still substantially less than exposures through food, dermal exposures from lawn uses of carbaryl dominate the residential pathway. Exposures through drinking water exposures are smaller than exposures through both the food and residential pathways with MOEs exceeding 15 for all scenarios.

Conclusion:

The Agency has developed a highly refined and complex cumulative risk assessment for the NMCs that represents the state of the science regarding existing hazard and exposure data and the models and approaches used. Interpretation of the risk estimates presented in this revised NMC CRA depends upon the synthesis and processing of a vast body of data on hazard and exposures. No single value in the assessment should be used to independently arrive at the interpretation of the risk estimates or results. EPA continues to have confidence -- as demonstrated by this assessment -- in the overall safety of our food supply.



Sensitivity analyses performed by the Agency were designed to evaluate the degree to which key areas of the risk assessment may or may not under- or over-estimate the cumulative risk in an effort to characterize and understand the MOEs estimated in this assessment. The sensitivity analyses demonstrate that the Agency has not under-estimated exposures and associated risks. Also, the Agency has elected to use 10% inhibition in brain AChE as the response level for the RPFs and PoDs. The 10% response level is health protective in that no functional or behavioral effects have been noted at or below this level in adult or juvenile animals. Thus the 10% response level provides a point where functional or behavioral neurotoxicity is not expected.

The Agency has undertaken extensive risk mitigation and risk reduction efforts over the last several years for many NMCs through the single-chemical aggregate risk assessments and notes that the risk mitigation efforts of the past several years have significantly reduced risk from exposures to the NMCs through food and drinking water and from residential use in the U.S. Based on these efforts, the cumulative risks from food, water, and residential exposure to NMCs do not exceed the Agency's level of concern. Taking into account these reductions and acknowledging that several key assumptions are designed to minimize the potential for this cumulative assessment to underestimate exposure and risk, the Agency concludes that -- based on the results of the revised NMC CRA -- there is a reasonable certainty that no harm will result from exposure to the NMC pesticides covered by this assessment, taking into account the cumulative effects of such residues. Accordingly, the pesticide tolerances for the NMCs covered by this risk assessment are considered to be "safe" as defined in FFDCA section 408(b)(2)(A) and to be reassessed for purposes of FFDCA section 408(g).



LIST OF ACRONYMS

AChe	Acetylcholinesterase
BMD	Benchmark dose (or BMD ₁₀)
BMDL	Lower limit on the benchmark dose (or BMDL ₁₀)
CAG	Cumulative Assessment Group
CARES	Cumulative and Aggregate Risk Evaluation System
CELS	Comparative Effect Levels
CFSAN	Center for Food Safety and Applied Nutrition
CGCM	Center for Golf Course Management
CHAD	Consolidated Human Activity Database
ChE	Cholinesterase
CMG	Common Mechanism Group
CNS	Central Nervous System
CRA	Cumulative Risk Assessment
CSFII	USDA Continuing Survey of Food Intake by Individuals
CWS	Community Water Systems
DEEM-FCID	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
EFED	Environmental Fate and Effects Division
EFH	Exposure Factors Handbook
EPA	Environmental Protection Agency
FCID	Food Commodity Intake Database
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
GoF	Goodness of Fit
HCl	Hydrochloride
HED	Health Effects Division
HSRB	Human Studies Review Board
IREC	Interim Re-registration Eligibility Decision
LCO	Lawn Care Operator
LN	Lognormal
LOAEL	Lowest Observable Adverse Effect Level
LOC	Level of Concern
LOD	Limit of Detection
LOQ	Limit of Quantification
MBS	Market Basket Study
MOE	Margin of Exposure
MRID	Master Record Identification Number
NASS	National Agricultural Statistics Survey
NHANES	National Health and Nutrition and Examination Survey
NHANES III	Third National Health and Nutrition Examination Survey



NAWQA	USGS National Water-Quality Assessment
Program	
NHEXAS	National Human Exposure Assessment Survey
NHGPUS	National Home and Garden Pesticide Use Survey
NMC	N-Methyl Carbamate
NMC CRA	N-Methyl Carbamate Cumulative Risk Assessment
NOAELs	No-Observed-Adverse-Effect-Levels
OPs	Organophosphorus Pesticides
OP CRA	Organophosphorus Pesticide Cumulative Risk
Assessment	
OPP	EPA's Office of Pesticide Programs
ORETF	Outdoor Residential Exposure Task Force
ORD	Office of Research and Development
PBPK	Physiologically Based Pharmacokinetic
PCA	Percent Crop Area
PCO	Pest Control Operator
PCRA	Preliminary Cumulative Risk Assessment
PDP	USDA's Pesticide Data Program
PoD	Point of Departure
PK	Pharmacokinetic
PNS	Peripheral Nervous System
PRZM-EXAMS	Pesticide Root Zone Model- Exposure Analysis Modeling System
RBC	Red Blood Cell
RED	Re-registration Eligibility Decision
REJV	Residential Exposure Joint Venture
RPF	Relative Potency Factor
RTU	Ready-to-Use
SAP	Scientific Advisory Panel
SHEDS	Stochastic Human Exposure and Dose Simulation
SLN	Special Local Need
SOP	Standard Operating Procedure
TC	Transfer Coefficient
TDS	Total Diet Study
TTR	Turf Transferable Residues
UE	Unit Exposure
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
WOE	Weight of the Evidence

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I. NMC Cumulative Update

A. Introduction

Background

The Food Quality Protection Act (FQPA) of 1996 significantly amended the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). One of the major changes imposed by FQPA was to require EPA to consider the cumulative effects of chemicals with a common mechanism of toxicity in its tolerance reassessment decisions.

In 2001, EPA concluded that the *N*-methyl carbamate (NMC) pesticides share a common mechanism of toxicity. This common mechanism group (CMG) was established based on the shared structural characteristics and similarity and their shared ability to inhibit acetylcholinesterase (AChE) by carbamylation of the serine hydroxyl group located in the active site of the enzyme (USEPA, 2001a). For this group of pesticides, recovery typically occurs rapidly (minutes to hours) following maximal inhibition of cholinesterase (ChE). In a February 4, 2004 Federal Register notice, EPA announced the members of the Common Assessment Group (CAG) (FR Vol.69, No.23, p. 5340-5344). These ten carbamates all display ChE-inhibiting activity, have current active registrations, and are expected to contribute to the carbamate cumulative risk through quantitatively meaningful exposure scenarios. The ten members of the CAG for the *N*-methyl carbamates and those chemicals which are included in the quantitative cumulative risk assessment are listed in the risk assessment.



Table I.[STYLEREf 2 \s]. Summary Information Regarding the NMC Pesticides and the Uses, Routes and Pathways Included in the NMC Cumulative Risk Assessment

Pesticide	Pesticide Uses	Pesticide Pathways			Pesticide Routes		
		Food	Drinking Water	Residential	Oral	Dermal	Inhalation
Carbaryl	Ag Crops	X	X		X		
	Lawn			X	X	X	X
	Garden			X		X	X
	Ornamentals			X		X	X
	Fruit Trees			X		X	X
	Pet Collar			X	X	X	
	Golfer Exposure			X		X	
Aldicarb	Ag Crops	X	X		X		
Oxamyl	Ag Crops	X	X		X		
Formetanate HCl	Ag Crops	X	X		X		
Methomyl	Ag Crops	X	X		X		
Carbofuran	Ag Crops	X	X		X		
Propoxur	Food Uses	X			X		
	Pet Collar			X	X	X	
Methiocarb	Ag Crops	X			X		
	Ornamental			X		X	X
Thiodicarb	Ag Crops	X	X		X		
Pirimicarb	Ag Crops	X			X		

To meet the requirements of FQPA, EPA developed methodologies for conducting cumulative risk assessments. As part of this process, EPA consulted with the FIFRA Scientific Advisory Panel (SAP) to obtain expert review, advice, and recommendations at each major step in the development of the underlying methodologies for cumulative risk assessments. EPA held numerous external peer-review meetings with the SAP and asked for comment on many issues, including its approaches to grouping chemicals based on a common mechanism of toxicity; Office of Pesticide Program's (OPP) guidance for conducting cumulative risk assessment; methods and approaches for dose-response and exposure assessment; and probabilistic exposure models for combining food, drinking water, and residential exposure pathways. In addition, the Agency also held numerous meetings with the FQPA Federal Advisory Committees TRAC (Tolerance Reassessment Advisory Committee) and CARAT (Committee to Advise on Reassessment and Transition), which were established under the Federal Advisory Committee Act (FACA). Various stakeholders including public interest groups, state agricultural agencies, pesticide industry representatives, growers, United States Department of Agriculture (USDA), and others were represented on these committees. In addition, numerous public technical briefings on each component of the cumulative methodology were held. In short, the Agency sought and received



advice, comments, and recommendations on the methodologies and framework that were to guide the implementation of FQPA and tolerance reassessment.

Based in part on the above consultations, OPP developed and published guidance on conducting cumulative risk assessments ("Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity") which is available on EPA's website at [[HYPERLINK "http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf"](http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf)]. This guidance has been reviewed by the FIFRA SAP and describes key principles for conducting these risk assessments. One such principle is the need to consider the time frame of both the exposure (e.g., When does exposure occur? What is the exposure duration?) and the toxic effect (e.g., What are the time-to-peak effects and the time to recovery? How quickly is the effect reversed?). Both should be adequately considered so that an individual's exposure is matched with relevant and appropriate toxicological values in terms of duration and timing. Inhibition of ChE caused by the *N*-methyl carbamates is followed by rapid recovery within minutes to hours. This rapid recovery is a unique characteristic of this group of pesticides and was considered and characterized as part of the risk assessment. Cumulative risk assessments should also account for temporal aspects of exposure, such as those related to the time of year during which applications resulting in exposures are likely to occur, the frequency of application, and the period of reapplication. Moreover, these assessments must appropriately consider age-dependent and demographic factors and patterns. The Agency's approach to each of these challenges in the cumulative hazard, exposure, and risk assessment is described throughout the document.

This cumulative assessment is intended to identify major sources of risk that could potentially accrue due to the use of a variety of pesticides which act through a common mechanism of toxicity. Regulatory decision making is based on the many detailed aspects of the single-chemical aggregate risk assessment. Because of the requirement that many data sets be combined into a single assessment, reducing the impact and likelihood of compounding conservative assumptions and over-estimation bias becomes very important in constructing the cumulative risk assessment. As a result, OPP has chosen to work with those data that most closely reflect likely exposures and not to incorporate those data that are inherently conservative by their nature (e.g., field trial data which incorporate maximum application rates and minimum pre-harvest intervals). These principles are fully described and laid out in the aforementioned guidance document.

EPA previously released the "Estimation of Cumulative Risk from *N*-methyl Carbamate Pesticides: Preliminary Assessment" in August 2005. During the period since the issuance of the preliminary cumulative risk assessment, the Agency has been working to further improve and refine its assessment of the cumulative risks associated with the NMC pesticides. These refinements



include changes to: incorporate the most recent food residue data by including pesticide residue data through 2006 from USDA's Pesticide Data Program; reflect the Agency's review of new toxicity data in juvenile animals; and to incorporate human data for certain NMC pesticides. In addition, the Agency has updated the assessment to reflect individual risk mitigation measures and other use pattern changes for individual NMC pesticides since the preliminary NMC CRA was issued in August 2005. Specifically, during this period, the Agency imposed risk reduction measures on some of the major contributors to carbamate cumulative risk, as discussed below. The risk estimates presented in the revised NMC CRA reflect the risk mitigation measures taken on individual carbamates since FQPA was signed into law in August 1996. A table summarizing these mitigation measures is provided in Appendix II.A. In general, EPA's risk estimates reflect risk mitigation measures that EPA determined to be warranted based on its assessment of the single chemical's risks. For all of the risk mitigation measures that are reflected in this document, EPA has commenced the processes necessary to implement its selected risk mitigation, but may not yet have completed these processes. Having already determined that risk mitigation is warranted for the individual chemical, EPA has chosen to exclude it from this assessment to avoid any confusion that yet further mitigation might be warranted solely on that basis, either for the individual chemical or for other NMC chemicals. Rather, where the risks are adequately addressed by previously identified risk mitigation, it was considered to be unnecessary to confirm that here. To the extent that any risk mitigation measures are not subsequently implemented as envisioned in this assessment, the revised NMC CRA will be revised as necessary. The following summarizes the major mitigation actions that the Agency has recently or will be taking with respect to registration of uses which have been excluded from the revised NMC CRA:

Carbofuran. In July 2006, the Agency issued its proposed decision to cancel all domestic uses of Carbofuran; only four import tolerances, (coffee, bananas, sugarcane, and rice) would remain. A Federal Register (FR) notice announcing this decision and soliciting public comments was published on August 30, 2006.

Any cancellation hearing for EPA's proposed decision on carbofuran would be scheduled to commence in 2008, which is after the issuance of this document. If all remaining uses of carbofuran are not cancelled after conclusion of a cancellation hearing, this assessment will be revised as necessary.

Methomyl. The methomyl registrant submitted a letter requesting the voluntary cancellation of the strawberry use on January 4, 2007. A Federal Register notice announcing the receipt of this request to delete the methomyl strawberry use published on April 25, 2007 (72 FR 20541) (FRL-8125-6). The public comment period for this notice closes on October 22, 2007.



A letter requesting voluntary cancellation of the use of methomyl on grapes was received from the registrant on September 14, 2007. A Federal Register notice announcing the receipt of this request will be published in October 2007. Based on these voluntary cancellations, the use of methomyl on grape and strawberry has been excluded from the *N*-methyl carbamate cumulative risk assessment.

Propoxur. In February 2007, the propoxur registrant submitted a letter requesting the voluntary cancellation of the all indoor spray uses that may result in non-occupational exposure for children. A Federal Register notice announcing this voluntary cancellation and soliciting public comments was published on April 25, 2007 (72 FR 20541) (FRL-8125-6). In July 2007, the Agency issued its Final Use Termination Order for Propoxur Residential Spray Use (EPA Registration Number 432-1288) for the use of propoxur, when formulated into a product that can be used as a spray on residential indoor use sites. The Agency has evaluated *N*-methyl Carbamate cumulative risks in a manner that *excludes* these crack and crevice-type residential uses so as to reflect the Agency's final termination order.

Aldicarb. In September 2007, EPA completed the Aldicarb Reregistration Eligibility Decision (RED). The Agency identified potential human health risks of concern associated with the current registered uses of aldicarb from drinking water exposure, and potential environmental risks of concern to birds, mammals and fish. To reduce these potential exposures and to address current risks of concern, EPA -- in agreement with the technical registrant of aldicarb -- will implement certain label restrictions. To address groundwater contamination concerns, the Agency will increase drinking water well set-backs for applications to peanuts in the southeastern coastal plains when certain criteria are triggered. In addition, to reduce environmental concerns, the Agency will implement application rate reductions and restrictions, state limitations, label amendments, and cancellation of certain commodities. EPA is also requiring data to confirm the decisions presented in the Aldicarb RED which and will seek public comment on the decisions in the RED in October 2007.

The current document is presented in three major parts:

- Part I: Revised NMC Cumulative risk assessment
- Parts II and III: Appendices which provide background material, additional graphs, and more technical and/or extensive details surrounding the analyses contained in Part I



Part I is divided into eight chapters. Chapter A is this general introduction. The following chapter (I.B), presents the Hazard Assessment with specific discussion of the Relative Potency Factor approach and empirical dose-response and time course modeling used to estimate relative potency. The next three chapters (C, D, and E) focus on each of the major exposure pathways (food, residential, and drinking water, respectively), including a discussion of assumptions, data inputs, and interrelationships of exposure data. Each of these pathways has unique issues relating to availability of data, scale, and interpretation of results. Results of each aspect of the assessment are discussed in these chapters with particular attention given to how they reflect potential exposures to the population and what might be inferred with regard to significant exposure pathways/scenarios. Chapter F of the document examines the results of combining estimates of risk from all sources of exposure, in a multi-pathway, probabilistic cumulative assessment, and further discusses the interpretation of the outputs with respect to the most significant pathways and scenarios. The results in this chapter were generated by the DEEM/Calendex software. Chapter G of this document is a risk characterization, which further discusses and characterizes the inputs to the assessment as well as the resulting model exposure estimates. Chapter H of this document provides references for the material cited in Parts A through G.



B. Hazard Relative Potency Factors

1. Introduction

OPP designated the NMC pesticides as a common mechanism group (USEPA, 2001a) based on the shared structural characteristics and similarities and their shared ability to inhibit AChE by carbamylation of the serine hydroxyl group located in the active site of the enzyme. Following maximal inhibition of cholinesterase, recovery typically occurs rapidly (minutes to hours). Pharmacokinetic data are only available for one NMC (i.e., carbaryl). Consequently, a multi-chemical, multi-pathway physiologically based pharmacokinetic (PBPK) model cannot be developed at this time for the NMC cumulative risk assessment (Appendix II.B.6). Therefore, the 2007 revised cumulative risk assessment relies on the relative potency factor (RPF) method for quantifying chemical potency. In the RPF approach, the toxic potency of each chemical is determined. A member of the cumulative assessment group (CAG) is selected as the index chemical which is used as the point of reference for standardizing the cholinesterase inhibiting potency of the other chemical members of the CAG. In the case of the NMC CRA, oxamyl is used as the index chemical.

The FIFRA SAP supported the scientific approach employed in the NMC cumulative hazard in the February and August 2005 meetings. EPA has considered the comments collected from the SAP as well as the registrants' error-only comment phase in July 2005 in the development of the current revised NMC CRA. The revised NMC CRA incorporates additional data available since the 2005 preliminary CRA in addition to uncertainty factors for the inter- and intra-species factor and FQPA 10X safety factor. Specifically, the Agency has included comparative cholinesterase data in juvenile (post-natal day 11 [PND 11] and PND17) and adult rats for six chemicals as well as cholinesterase inhibition and recovery data from human subjects for three chemicals. The comparative cholinesterase data are used here to inform the FQPA 10X factors while the cholinesterase data in human subjects has been used to form the inter-species factor in the revised CRA. It is noted that carbofuran has been ruled ineligible for reregistration and is undergoing the process of cancellation. However, for completeness and because tolerances for bananas, coffee, rice and sugarcane will continue for import purposes, the hazard chapter includes RPFs and uncertainty factor information for carbofuran.

This cumulative hazard assessment represents the collaborative efforts of scientists from OPP and EPA's National Health and Environmental Effects Research Laboratory (NHEERL) and National Center for Computational Toxicology (NCCT). The purpose of this hazard chapter is to describe EPA's approach for:



- ☐ Determination of the relative cholinesterase inhibiting potency and half-life to recovery used for each *N*-methyl carbamate in the CAG;
- ☐ Selection of the index chemical used as the point of reference to standardize the potency of each *N*-methyl carbamate;
- ☐ Establishment of a baseline or reference value (i.e., points of departure) used to estimate potential risk for the group for each route of interest; and
- ☐ Identification of the intra-species, inter-species, and FQPA 10X safety factors used in this cumulative risk assessment.

2. Endpoints and Toxicology Studies

When using the RPF method and before the cumulative risk of exposure to the NMCs can be quantified, the relative toxic potency of each NMC must first be determined. The determination of relative toxic potency is calculated using a uniform basis of comparison, by using, to the extent possible, a common tissue, species, and sex for all the exposure routes of interest (USEPA, 2002a). NMCs exert their neurotoxicity by carbamylating the enzyme acetylcholinesterase (AChE) in both the central (brain) and peripheral nervous systems. Since cholinesterase (ChE) inhibition is the critical event in NMC toxicity, ChE inhibition provides the common endpoint for the revised NMC CRA. The available ChE activity measures provide a more uniform measure of toxicity compared to behavioral measures for performing cumulative risk assessment. Behavioral measures are often limited in terms of the scope of effects assessed and by the lack of standardization of laboratory equipment among laboratories. Moreover, behavioral changes in animal studies usually occur at similar or higher doses compared to doses needed to inhibit cholinesterase activity. In order to evaluate the concordance between ChE inhibition and behavioral endpoints, EPA has performed a series of dose-response and time course studies with seven NMCs where RBC and brain ChE, along with clinical signs ('tox' score) and motor activity, were measured (Appendix II.B.5; McDaniel *et al.*, 2007; Padilla *et al.*, 2007).

There are laboratory animal data on NMCs for cholinesterase activity in plasma, red blood cell (RBC), whole blood, and brain (whole brain and brain sections). Measures of ChE inhibition in the peripheral nervous system (PNS) are very limited for ChE inhibiting pesticides, in general. As a matter of science policy, blood cholinesterase data (plasma and RBC) are considered appropriate surrogate measures of potential effects on PNS acetylcholinesterase activity, and of potential effects on the central nervous system (CNS) when brain ChE data are lacking (USEPA, 2000a). Furthermore, when RBC ChE data are of adequate quality, as is the case for the NMCs, RBC ChE data are preferred over plasma ChE data. AChE is the target enzyme for this common mechanism group and is the primary form of ChE found in RBCs.



Butylcholinesterase (BChE) is the primary form found in plasma. Inhibition of BChE is considered a measure of exposure, but has not been shown to be of toxicological significance. Some studies with NMCs provided whole blood ChE. Whole blood ChE represents a mixture of plasma and RBC ChE, and thus may not provide a uniform endpoint for comparison across chemicals. Consequently, whole blood ChE data were not used in this assessment. In the case of brain ChE inhibition, data are available for each NMC with whole brain (or half brain). In some studies, brains were dissected into different brain areas (e.g., cerebellum). Because the brain dissections provided are not standardized across the studies and brain section data are not available for each NMC, these data do not represent a uniform basis of comparison. RBC and brain (namely whole, half) ChE inhibition were considered potential endpoints for extrapolating risk to humans in the revised NMC CRA. **As described in Section B.4 below, the Agency is using brain ChE data as the basis for RPFs and points of departure (PoD) in this assessment.**

Humans may be exposed to the NMCs through food and drinking water and in and around residences, schools, commercial buildings, etc. Therefore, the potency of NMCs needs to be determined for the oral, dermal, and inhalation routes of exposure. Under FIFRA, toxicity studies in various species (e.g., dog, mouse, rat, and rabbit) are submitted to OPP. For the NMCs, toxicity studies in the rat provide the most extensive and robust database of ChE inhibition data. Thus, the focus of this analysis was on ChE activity data derived from male and female (non-pregnant) rats. EPA used rabbit studies for pesticides with residential/non-occupational exposure potential when dermal toxicity data in rats were not available.

Toxicological characteristics of the NMCs involve maximal ChE inhibition followed by the rapid recovery, typically in minutes to hours. As such, the critical duration of exposure for this common mechanism group is acute ChE inhibition measured at the peak time of effect. Characterizing chemical specific recovery is critical for characterizing overlapping exposures and thus cumulative risk. EPA has compiled data from several different kinds of studies:

1. oral (gavage) studies quantifying the relationship between maximum inhibition from single or multiple administered dose(s) in adult rats;
2. oral (gavage) studies quantifying the *in vivo* recovery time course, usually at several doses, and beginning at or around the time of maximum inhibition (which had typically been determined in preliminary studies) in adult rats;
3. comparative cholinesterase assay (CCA) studies quantifying the ChE sensitivity of juvenile rats compared to adult rats; comparing dose-response and time to recovery in juvenile (PND11 and/or PND 17) and adult rats; and/or



4. oral double blind ascending studies quantifying the dose-response and recovery time course of ChE in humans; and,
5. inhalation and dermal studies for those pesticides with residential exposure.

Data included in the revised NMC CRA were extracted from studies submitted by pesticide registrants and from dose-response and time course studies performed by EPA's NHEERL. Table I.B-1 provides the list of various types of studies included in the analysis. Appendix [REF_Ref178093785 \r \h] contains the electronic spreadsheets of brain and RBC ChE data used.

Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Test guidelines/studies that contain evaluations for ChE activity.

Study Type	Guideline Type
Oral	
Acute oral toxicity study in rat	OPPTS 870.1000
Acute neurotoxicity in rat	OPPTS 870.6200a
Subchronic neurotoxicity in rat	OPPTS 870.6200b
Developmental neurotoxicity oral in rat	OPPTS 870.6300
Chronic oral toxicity in rat	OPPTS 870.4100
Range finding oral toxicity study in rat	Not applicable
Other/Special Studies	Not applicable
Dermal	
21/28-Day dermal toxicity in rat or rabbit	OPPTS 870.3200
Inhalation	
Acute inhalation in rat	OPPTS 870.1200
Chronic inhalation in rat	OPPTS 870.4100

In toxicology studies submitted to EPA for pesticide registration, measurements of cholinesterase inhibition are typically performed using some variation of the Ellman spectrophotometric method (Ellman *et al.*, 1961). Under standard conditions, this method usually involves extensive sample dilution, prolonged incubation, and temperatures around 37°C; all of which promote



reversal of the enzyme inhibition. If precautions are not taken to prevent recovery using this method, then reported cholinesterase activities can underestimate actual cholinesterase inhibition (Winteringham and Fowler, 1966; Williams and Casterline, 1969; Nostrandt *et al.*, 1993; Hunter *et al.*, 1997) which could have an impact on the relative potency estimates. A radiometric method such as that reported by Johnson and Russell (1975) provides the most appropriate method for measuring cholinesterase inhibition due to NMC exposure because factors which promote reversibility are minimized. The dilution is minimized (1:30 vs. more than 1:1000 dilution for the standard Ellman method), and incubation time may be more rapid for the radiometric method (one to three minutes compared to 10 minutes or greater). Furthermore, the radiometric method may be conducted at lower temperatures. The Ellman method can be modified to minimize conditions promoting reactivation. Reducing the tissue dilution, shortening the time, and lowering the temperature of the assay all limit the amount of spontaneous decarbamylation of the inhibited enzyme (Nostrandt *et al.*, 1993). Although modifications to the Ellman method are not standardized, when performed with the appropriate care, the modified Ellman method can provide reliable cholinesterase data.

To aid in the characterization of the cholinesterase data provided by the studies submitted for registration, scientists from EPA's NHEERL have systematically evaluated cholinesterase inhibition following acute exposures of adult rats to seven *N*-methyl carbamates (carbaryl, carbofuran, formetanate HCl, methomyl, methiocarb, oxamyl and propoxur) using both the standard Ellman and radiometric techniques. This work has been published in the scientific literature (Padilla *et al.*, 2007); the data from these experiments are also included in Appendix II.B.1. EPA's issue paper presented to the FIFRA SAP in February, 2005 provided graphical comparisons of the data from selected registration studies and EPA's radiometric experiments. These graphical comparisons showed good concordance between the registration data and EPA's radiometric experiments. In the current revised cumulative risk assessment, these data have been analyzed statistically (see section I.B.3). Overall, the results provided by the EPA radiometric studies provide similar benchmark dose estimates to the registration studies.

The laboratory protocols or standard operating procedures (SOPs) for some registration studies have been provided by the pesticide registrants. EPA has received protocols or SOPs for studies for nine of the ten NMCs. Methiocarb is the only chemical the Agency has not received a protocol or SOP for measuring cholinesterase activity. The protocols available indicate that the experimental conditions among laboratories vary but that dilutions are generally limited to approximately 1:20 and that samples are frozen immediately. Although information regarding the time of sample handling is more limited, the available information suggests that reasonable precautions were taken in these studies to reduce reactivation prior to analysis. The Agency considers the methods used to evaluate ChE activity in the laboratory to be a critical



component of the hazard assessment for the NMCs and will continue to evaluate SOPs as new studies are submitted in the future. A summary of the information provided in these protocols can be found in Appendix II.B.5.

A summary of the studies and endpoints included in the revised cumulative risk assessment for the NMCs are provided in Table [REF _Ref175636414 \h]. This table includes studies recently submitted, such as comparative cholinesterase studies and human studies reviewed and found to be ethically conducted and scientifically valid by the Human Studies Review Board (HSRB) in 2006.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. List of toxicity studies used in the Revised *N*-Methyl Carbamate Risk Assessment.

Chemical	Oral		Dermal		Inhalation	
	Study ID	ChE Inhibition Data	Study ID	ChE Inhibition Data	Study ID	ChE Inhibition Data
Aldicarb	43442305 ¹	Brain, RBC	No residential uses, thus data are not needed			
	43442302 ²	RBC				
	45079705	RBC				
	43829601	Brain, RBC				
	43829602	Brain, RBC				
	45068601 ³	Brain				
	45150701					
	46618001					
42373001	Human RBC					
Carbaryl	43845202	Brain, RBC	45630601 (47151902)	Brain, RBC (In vitro dermal penetration)	Inhalation data are not available	
	43845203	Brain, RBC				
	44122601	Brain, RBC				
	44393701	Brain, RBC				
	47007001/ 47143001	Brain, RBC (NHEERL CCA)				
	NHEERL Padilla et al., 2007	Brain, RBC				
	NHEERL 47143001	Brain, RBC comparative				
Carbofuran	45675701	RBC	No residential uses, thus data are not needed			
	46688912-14	CCA Brain				
	47143703-05	CCA Brain, RBC				
	Moser CCA	Brain, RBC				
	Padilla et al., 2007	Brain, RBC				
Formetanate	46618901	CCA Brain, RBC	No residential uses, thus data are not needed			
	Padilla et al., 2007	Brain, RBC				
Methiocarb	Padilla et al., 2007	Brain, RBC	40922301	Brain, RBC	Data are not available	
			41771701	Brain		



Chemical	Oral		Dermal		Inhalation	
Methomyl	44472001	Brain, RBC	No residential uses, thus data are not needed			
	44487501	Brain, RBC				
	46646401	CCA Brain, RBC				
	Padilla et al., 2007	Brain, RBC				
	44721401	Human RBC				
Oxamyl	44254401	Brain, RBC	40827601		45155801	Brain, RBC
	44472001	Brain, RBC				
	44420301	Brain				
	46615301	CCA Brain, RBC	44751201			
	Padilla et al., 2007	Brain, RBC				
	44912301	Human RBC				
Pirimicarb	44485301	Brain, RBC	No residential uses, thus data are not needed			
	44233103	RBC				
	00113638	Brain, RBC				
Propoxur	Padilla et al., 2007	Brain, RBC	41066001	Brain, RBC	42648001	Brain, RBC
Thiodicarb	45138702	RBC	No residential uses, thus data are not needed			
	45138703	Brain, RBC				

¹Brain and RBC data for parent only used in the analysis; ²Brain data at 24 hours not used in the analysis; ³MRIDs listed here are referenced in the Aldicarb oral rat brain ChE analysis in Appendix II.B.2 as: 1) 46618001 as Moser-1; 2) 45068601 as Moser-2; and 3) 45150701 as Moser-3.

3. Determination of Toxic Potency

As described in the guidance document for cumulative risk assessment (USEPA, 2002a), dose-response modeling is preferred over the use of NOAEL/LOAELs (i.e., no- or lowest-observed-adverse-effect-levels) for determining relative toxicity potency. NOAELs and LOAELs do not necessarily reflect the relationship between dose and response for a given chemical, nor do they reflect a uniform response across different chemicals. In the present analysis, benchmark dose (BMD) modeling has been used to determine the toxic potency of the NMCs. EPA's draft BMD guidance (USEPA, 2000d) suggests that the central estimate on the BMD provides an appropriate measure for comparing chemical potency and that the lower limit on the central estimate (i.e., BMDL) provides an appropriate measure for extrapolating risk. The 10% response level is generally at or near the limit of sensitivity for discerning a statistically significant decrease in ChE activity across the blood and brain compartments and is a response level close to the background ChE. As part of EPA's Revised Cumulative Risk Assessment for the OPs, EPA performed a power analysis of brain ChE data available for more than 30 OPs (USEPA, 2002b). The results of the analysis indicated that most studies can reliably detect 10% brain ChE inhibition. Furthermore, in studies submitted to EPA for pesticide registration, clinical signs and behavioral effects have not



been shown in studies with below 10% ChE inhibition. In this cumulative risk assessment, the central estimate of the BMD₁₀ was selected as the response level for developing RPFs. The lower limit on the BMD₁₀ (i.e., BMDL₁₀) was selected for the points of departure (PoDs). A PoD is a point estimate on the index chemical's dose-response curve that is used to extrapolate risk to the exposure levels anticipated in the human population.

The following section describes the empirical dose-response modeling performed for the NMCs. BMD₁₀ and BMDL₁₀ estimates for the NMCs are provided in Tables 1.B-3 thru 5. Half-life time to recovery for each of the NMCs is provided in Table 1.B-6. Detailed information about the empirical modeling for each chemical can be found in Appendix II.B.2.

a. Empirical Modeling: Dose-Time Response Model and Benchmark Dose Estimation

i. Dose-Time Response Model

Several features of the dose-time response for the *N*-methyl carbamates were to be captured in an empirical model:

- ☐ The rapid decline of ChE activity with increasing dose, perhaps after a "shoulder" at the low-dose end of the dose-response curve;
- ☐ A potential minimum level below which ChE activity will not drop, regardless of dose;
- ☐ The rapid decline of ChE activity after dosing to a minimum level which depends upon dose, then returns to the background level over a period of minutes to hours, at a rate that may also depend upon dose;
- ☐ Lack of early time points in most of the time course studies to accurately estimate the time of maximum effect, but instead start collecting data around a previously estimated time of maximum effect.

The model described is the result of multiplying a dose-response model for inhibition that is closely related to the model that was successful at characterizing OP dose-response curves (USEPA, 2002b) and a time-course model for inhibition. Transformations of parameters were used to enforce constraints, since the statistical software used for estimating model parameters does not incorporate bounded estimation (for example, to require that half-life estimates remain positive).

The model for inhibition, before parameters were transformed to enforce constraints, is



$$g(d) = g(d; R, P, D_R, \gamma) = (1 - P) \left(1 - e^{\log\left(\frac{1-R-P}{1-P}\right) \left(\frac{d}{D_R}\right)^\gamma} \right)$$

(Eq. 1)

where:

- ☐ d is administered dose, and is part of the data set;
- ☐ P is the minimum fraction of background ChE activity, and is constrained to fall between 0 and 1;
- ☐ R is the inhibition fraction associated with the desired benchmark dose (that is, the benchmark dose is the dose expected to yield $100 \times R\%$ inhibition at the time of maximum effect), and is set to 0.10 in this analysis;
- ☐ D_R is the benchmark dose, constrained to be greater than 0.0;
- ☐ γ is a shape parameter to allow a shoulder at the low-dose end of the dose-response curve, and is constrained to be greater than 0.0.

Two different time course models were used. One time course model is the difference of two exponential functions, scaled so that the maximum is always 1:

$$h(t) = h(t; T_A, T_R) = C_0 \left(e^{-\frac{\ln(2)t}{T_R}} - e^{-\frac{\ln(2)t}{T_A}} \right)$$

(Eq. 2)

where:

- ☐ T_A is the half-life of the process that results in an increase in inhibition, and
- ☐ T_R is the half-life of the process that results in a decrease in inhibition (recovery or reactivation).

The maximum of $h(t)$ occurs at:

$$T^* = \frac{T_R T_A (\ln(T_R) - \ln(T_A))}{\ln(2)(T_R - T_A)}$$

(Eq. 3)



so [EMBED Equation.DSMT4]

With this scaling, $h(t)$ is symmetric in the two parameters (that is, $h(t; a, b) = h(t, b, a)$), which complicates statistical estimation unless a constraint is added to keep $T_R > T_A$. Also, many data sets require that T^* be specified (not estimated from the data), because the designs were inadequate for estimating T^* . For these reasons, it is convenient to reparameterize the model in terms of T^* and $\alpha = T_R / T_A$ and make sure α is constrained to be greater than 1.0.

The design of most of the time-course datasets considered in this assessment did not allow clean estimation of both T^* and α , and the reparameterization sometimes increased the difficulty of estimation. Thus, an alternative, much simpler, time-course model was used in all but one of the dose-time studies (aldicarb, brain ChE). In this simpler model, ChE activity is taken to be described by an exponential recovery time-course, beginning at a time δ after dosing. This gives the following recovery function:

[EMBED Equation.DSMT4]

(Eq. 4)

where:

T_R is the half-life of recovery

δ is the difference in time between dosing and the first ChE measurement.

In this model, the only parameter to be estimated is T_R .

Multiplying $g(d)$ and $h(t)$ together gives a function for ChE inhibition as a function of dose and time. Thus, Equation 5

$$f(t, d) = A \times (1 - g(d) \times h(t))$$

is a model for ChE activity as a function of dose and time, where A gives the background (that is, control) level of ChE activity.

There were no time-course data for any of the dermal and inhalation data sets, so the above model was simplified for those sets, either by setting the time course parameters to a fixed value, or by fitting a linear model to the natural logarithm of ChE activity, which is equivalent to an exponential dose-response model when the variance is proportional to the square of the mean ChE activity level (that is, the coefficient of variation is constant across doses).



The following transformations were used to ensure that parameters remained in their permitted range:

- ☐ $lA = \ln(A)$, to force $A > 0$
- ☐ $ID = \ln(D_R)$, to force $D_R > 0$
- ☐ $tz = -\ln((1 - R - P)/P)$, to force $0 < P < 1 - R$
- ☐ $lg = \ln(\gamma)$, to force $\gamma > 1$
- ☐ $lTr = \ln(T_R)$, to force recovery half-life > 0 (in simplified time-course model)
- ☐ $IdT = \ln(\alpha)$, to force $T_R > T_A$
- ☐ $IT_{max} = \ln(T_{max})$, to force $T_{max} > 0$.

ii. Statistical Methodology

The statistical model fit to the dose or dose-time response data depended on whether the experimental design involved repeated measures (some RBC studies only) or not. The most general model fit to the ChE activity data was (for the simplified time course model), for individual j in study i , with sex $s(j)$ at time t_{jk} :

$$y_{ijk} = f(t_{jk}, d_{ij}; lA_{is(j)}, lD_{is(j)}, tz, lg, lTr_d, delta) + \varepsilon$$

$$\varepsilon \sim N(0, \sigma_{is(j)}^2 \{f(\dots)\}^q)$$

When there was more than one study,

$$lD_{is(j)} \sim N(ID_{s(j)}, \sigma_D^2),$$

that is, the log BMD was taken to be normally distributed around a mean that possibly differed between sexes.

When there were repeated observations on a subject, the logarithm of individual animals background ChE activity levels were assumed to be normally distributed about a mean that varied between sexes, studies, and, when there



were controls at all times, among times (this latter allows for the possibility of variation among analytic batches, if samples from the same time post dosing were analyzed as a batch).

$$IA_{ts(j)jk} \sim N(IA_{ts(j)k}, \sigma_A^2),$$

When recovery time-course data were available, the recovery half-life was allowed to differ among the doses for which recovery data were available. Often for a chemical, some datasets were just dose response studies conducted around the time of maximum inhibition, and others included a recovery phase, with samples taken every few hours or more frequently. In this case, the range of doses in all the studies together was grouped so that one dose with a time-course was included in each group. This allowed the estimate of recovery half-life to change with dose when the right data were available. However, often a chemical had recovery time course data for only a single dose level, so only a single recovery half-life could be estimated.

The process of estimating parameters proceeded in three steps. First, initial values for the parameters were arrived at using the R function `getInitialValues` (included in the library `DRUtils`). This function provides a graphical interface that allows the user to quickly arrive at reasonable estimates for the parameters, and allows a few iterations of an optimization algorithm to improve those initial estimates, using ordinary least squares as an objective function. Based on these initial estimates, the degree to which it would be possible to uniquely estimate the model parameters was determined, by analyzing the condition number of the matrix of gradient of the model with respect to the model parameters, and of the matrix of (unscaled) variances and covariances of the parameters, evaluated at the data points (times, doses, sexes) in all the data sets. At this point, it was often possible to simplify the model by noticing that it was impossible to determine a unique value for, for example tz , because doses did not go high enough for inhibition to approach its maximum value, or the maximum level of inhibition was 100%.

The next step was to determine an appropriate model for the error variance. The options considered were either; a constant variance, a constant variance that differed among studies and sexes, or a variance that was proportional to a power of the mean ChE activity level, and whose constant of proportionality varied among studies and between sexes. This was determined by fitting either a cell mean model (with indicator functions identifying individual dose X time X sex X study groups) or, more commonly, fitting the full nonlinear dose-time model using generalized nonlinear least squares (Pinheiro and



Bates, 2000). In either case, likelihood ratio tests were used to identify the variance model to use (Pinheiro and Bates, 2000).

Using that variance model, a full version of the dose-time course model was fit to the data, and contrasts used to determine whether *ID* needed to differ among sexes. Pinheiro and Bates (2000) note that likelihood ratio tests for fixed effects in mixed effects models tend to reject the null hypothesis enthusiastically, whereas using contrasts to test parameter values comes close to the nominal type I error rates.

Finally, a simplified model was fit to the data, and the resulting parameter estimates used to determine the values of *ID* and *ITr* and their standard errors. BMDs were calculated as $\exp(ID)$, and BMDLs were calculated by exponentiating the lower end of a two-sided 90% confidence interval for *ID*.

All statistical analyses used the statistical software environment R (version 2.0.1, patched version of 2005-01-26; R Development Core Team, 2004) and its associated packages. Appendix II.B.3 contains the computer code used in EPA's analyses.

b. Results: Benchmark Dose and Potency Estimation

Results of the empirical dose-response modeling are provided below. Detailed descriptions of the analysis and results of empirical dose-response modeling for each chemical are provided in Appendix II.B.2.

The oral BMD_{10s} for the NMCs range across several orders of magnitude with aldicarb and pirimicarb representing the most and least potent pesticides, respectively, for both brain and RBC ChE inhibition. The number of studies available for analysis varies among the chemicals (Table 1. B-2). At least two studies containing RBC and whole brain ChE inhibition in male and female rat were available for eight of ten NMCs (aldicarb, carbaryl, carbofuran, formetanate HCL, oxamyl, methomyl, pirimicarb, and thiodicarb). At present time, the only RBC and whole brain ChE data for methiocarb and propoxur are from EPA's NHEERL dose-response and time course studies in male rats (Padilla *et al.*, 2007).

For those chemicals that have data in male and female adult rats, EPA analyzed both sexes. When male and female data provided statistically similar BMD_{10s}, the data were combined and analyzed jointly. This joint analysis provides a more robust analysis using all the available data. In cases where the BMD estimates were statistically different, sex specific BMD_{10s} are presented ([REF _Ref175637544 \h], and Table 1.-5, below). As mentioned above, only male data are available for two NMCs (methiocarb, propoxur). Reliable BMD₁₀ estimates for RBC ChE inhibition from pirimicarb could not be



calculated due to a lack of response even at the highest doses tested (110 mg/kg).

ChE inhibition measured using both radiometric and modified Ellman techniques are available for aldicarb, carbaryl, carbofuran, formetanate HCl, methomyl, and oxamyl. RBC and brain ChE data from the two methods provided statistically similar BMD₁₀ estimates for all of the chemicals and were combined in the analysis to provide a more robust potency estimate. As shown in Table I.B-3, for carbaryl, both methods provided similar BMD₁₀ estimates for RBC ChE. However, for brain ChE in males, the BMD₁₀ estimated from EPA's radiometric study is larger than that estimated from the studies using modified Ellmans. Four registration studies were included in the analysis (MRID nos. 43845202, 43845203, 44122601, 44393701). For all four studies, Sprague-Dawley rats were administered via gavage with an aqueous vehicle of 0.5% (w/v) carboxymethyl-cellulose (high viscosity)/0.1% (w/v) Tween 80 (10mL/kg). EPA's experiments involved Long Evans rats dosed via gavage with corn oil (1 mL/kg) as the administration vehicle. Given that each of the carbaryl studies provided valid and acceptable ChE data, there is no scientific support for removing any studies from the analysis. Thus, the Agency has decided to include all the available brain ChE data in the carbaryl BMD₁₀ estimate used for potency determination (i.e., registration combined with Padilla data of 1.6 mg/kg).



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Oral BMD₁₀s and BMDL₁₀s from rat brain and RBC ChE inhibition for the *N*-methyl carbamates

Chemical	Brain		RBC	
	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)
Aldicarb	F= 0.05 M= 0.06	F= 0.03 M= 0.03	0.03	0.02
Carbaryl	Registration F= 1.60 Registration M= 1.21 NHEERL M=5.46 Combined M=1.58 Moser = 2.63	Registration F= 1.35 Registration M= 0.99 NHEERL M= 4.15 Combined M= 1.11 Moser = 2.03	Reg. =5.59 Moser = 0.96	Reg. = 3.41 Moser = 0.73
Carbofuran ²	0.10	0.0873	0.03	0.01
Formetanate HCl ²	0.11	0.06	0.09	0.03
Methiocarb ²	1.31	0.56	3.18	0.81
Methomyl	0.36	0.2677	0.20	0.11
Oxamyl	0.24	0.18	0.28	0.16
Pirimicarb	11.96	6.98	NA	NA
Propoxur ²	2.09	0.83	1.54	0.28
Thiodicarb	0.27	0.23	1.39	0.90

¹BMD estimates are presented as a single estimate when there are no differences between sexes and between the radiometric and modified Ellman methods, unless otherwise noted.

²BMD estimates are for male only

NA: No relationship between RBC ChE activity and pirimicarb dose.

Figure I.[STYLEREf 2 \s]-[SEQ Figure * ARABIC \s 2]. Plot of BMD₁₀s and the 95% confidence limits for rat brain ChE inhibition for the *N*-methyl carbamates

[EMBED SigmaPlotGraphicObject.4]

Figure I.[STYLEREf 2 \s]-[SEQ Figure * ARABIC \s 2]. Plot of BMD₁₀s and the 95% confidence limits for rat RBC ChE inhibition for the *N*-methyl carbamates¹

[EMBED SigmaPlotGraphicObject.4]

¹BMD₁₀/ BMDL₁₀ for RBC ChE were not developed for pirimicarb; no dose-response relationship was observed up to highest dose tested (110 mg/kg).

Potency estimates (BMDs) used for calculating dermal and inhalation RPFs are provided in Tables 1.B-4 and 1.B-5. Dermal and inhalation RPFs are



needed for carbaryl, methiocarb, and propoxur as these have residential uses. Sufficient dose-response data were available for carbaryl to calculate BMD₁₀ estimates for RBC and brain ChE via the dermal route. As for the dermal studies with methiocarb and propoxur, no ChE inhibition was observed up to the highest doses tested. The highest doses in the methiocarb and propoxur studies have been used to estimate dermal relative potency.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Dermal BMD₁₀s, BMDL₁₀s, and potency estimates from rat and rabbit brain and RBC ChE inhibition for the *N*-methyl carbamates with residential/non-occupational uses¹

Chemical	Brain		RBC	
	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)
Carbaryl ²	49.35 ³	30.56	F= 86.18 M= 59.04	F= 60.55 M= 46.91
Methiocarb ⁴	375 ⁵			
Propoxur ⁴	1000 ⁵			

¹ See Table I.B.7 for brain BMD₁₀s and BMDL₁₀s for oxamyl; ²Data from rat studies; ³Comparative In vitro dermal penetration data were NOT used to refine the brain BMD; ⁴Data from rabbit studies; ⁵Dermal endpoint is based on the highest dose tested in the dermal study; No ChE inhibition was observed at any dose.

Rat inhalation data with propoxur were available to estimate a BMD₁₀ for brain ChE. Inhalation studies with carbaryl and methiocarb are not available at this time. However, dose-response and time-course data via the inhalation route were requested for carbaryl as part of the carbaryl IRED. Route specific studies are preferred since they account for route specific kinetic characteristics which may impact chemical potency. In the absence of inhalation studies, oral data are being used in the revised cumulative risk assessment to estimate inhalation relative potency for carbaryl and methiocarb. This introduces uncertainty regarding the estimation of cumulative risk for the inhalation pathway. However, given that these chemicals do not have a port of entry effect, are expected to be rapidly absorbed, and do not require activation, ChE measured from oral studies are not expected to substantially underestimate potency. (Note: Data from dermal and inhalation studies with oxamyl are not provided here because oxamyl does not have residential uses. See Section II.B.5 for selection of index chemical [oxamyl]).



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Inhalation BMD₁₀s, BMDL₁₀s, and potency estimates from rat brain and RBC ChE inhibition for the *N*-methyl carbamates with residential/non-occupational uses

Chemical	Brain		RBC	
	BMD ₁₀	BMDL ₁₀	BMD ₁₀	BMDL ₁₀
Carbaryl ¹	1.58 mg/kg	1.11 mg/kg	5.59 mg/kg	3.41 mg/kg
Methiocarb ¹	1.31 mg/kg	0.56 mg/kg	3.18 mg/kg	0.81 mg/kg
Propoxur ²	F= 0.0095 mg/L M= 0.016 mg/L (converted to 4.54 mg/kg for RPF calculation)	F= 0.0076 mg/L M= 0.011 mg/L	NA	NA

¹No inhalation studies are available for carbaryl and methiocarb; potency estimates are from oral studies

²Inhalation BMDs and BMDLs for propoxur were different between sexes, therefore are displayed separately. No apparent dose-response for RBC inhalation for propoxur and therefore no BMD.

c. Results: Half Life Time to Recovery

Half-lives for time to recovery from oral studies in adult rats are provided in Table I.B-6. Since brain ChE is the focus of this revised assessment and the preliminary assessment indicated similar recovery for brain and RBC ChE, Table I.B-6 provides only brain half-life estimates. For most of the NMCs, recovery half-life estimates for brain AChE inhibition range from <1 hour up to 4 hours for adults. Recovery half-lives increased with dose for brain AChE in carbaryl studies. No significant sex differences were noted in brain AChE recovery half lives. At higher doses of carbaryl, recovery half-life for oral exposure was estimated to approximately 12 hours. However, at lower doses more relevant for risk assessment purposes, the half-life for carbaryl cholinesterase inhibition was estimated at 1 to 2 hours.

For those NMCs which have data in male and female adult rats, the Agency analyzed both sexes. When male and female data provided statistically similar BMD₁₀s, the data were combined and analyzed jointly. This joint analysis provides a more robust analysis using all the available data. However, female data are not available for methiocarb and propoxur while *in vivo* recovery time course data were not sufficiently robust to estimate brain cholinesterase half-lives for pirimicarb and thiodicarb. Overall, the half-life to recovery data support the use of acute, single day exposures in the NMC cumulative risk assessment.



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Half-life for time to recovery for adult rats from oral studies for brain ChE inhibition for the *N*-methyl carbamates¹

Chemical	Brain	
	Recovery Half-Life Estimate (hrs)	Lower & Upper Confident Intervals (hrs)
Aldicarb	1.52	1.16-1.99
Carbaryl	1.83	1.23-2.72
Carbofuran	NHEERL 1.65 Registrant 0.68	NHEERL 1.04-2.62 Registrant 0.54-0.86
Formetanate HCL	4.26	3.32-5.460
Methiocarb ²	2.77	1.91-4.01
Methomyl	Registrant (F) 0.67 Registrant (M) 1.05 NHEERL (M) 0.70	Registrant (F) 0.55-0.98 Registrant (M) 0.91-1.23 NHEERL (M) 0.50-0.98
Oxamyl	(F) 0.93 (M) 0.70	(F) 0.78-1.11 (M) 0.58-0.856
Pirimicarb	NA ³	NA
Propoxur ²	2.69	1.02-7.04
Thiodicarb	NA	NA

¹Recovery half-life estimates are presented as a single estimate when there are no differences between sexes and between radiometric and modified Ellman methods, unless otherwise noted; ² Half-life estimates are for males only; ³NA: insufficient time course data to estimate brain cholinesterase half-life.

4. Selection of Relative Potency Factors: Brain ChE Inhibition

A key component of cumulative hazard assessment is to select an endpoint pertinent to the common mechanism of toxicity that can be used to quantify cumulative risk. EPA is quantifying cumulative risk to the NMCs using RPFs and PoDs from brain ChE data. As mentioned above, in cases where male and female rats provide similar BMD₁₀ estimates, EPA has developed potency estimates jointly (methomyl, pirimicarb and thiodicarb). At the present time, only male data are available for methiocarb, and propoxur. For NMCs where the female and male data provided statistically different results (aldicarb,



carbaryl), the male BMD₁₀ has been used to calculate relative potency factors since it was the more health protective (i.e., lower) value.

As shown in Table I.B-3, BMD₁₀ estimates of brain ChE inhibition were generally similar to those for RBC ChE data. For nine of the ten NMCs (including the most potent NMCs), brain ChE is equally sensitive or more sensitive compared to RBC ChE inhibition. Thus, brain ChE inhibition data provides a health protective endpoint for estimating cumulative risk on both the central and peripheral nervous system. Compared to BMD₁₀ estimates based on RBC ChE, BMD₁₀ estimates based on brain ChE have tighter confidence intervals and therefore will confer less uncertainty on cumulative risk estimates. Moreover, brain ChE inhibition represents a direct measure of the common mechanism of toxicity as opposed to using surrogate measures (e.g., blood measures).

5. Selection of the Index Chemical (Oxamyl)

OPP's cumulative risk assessment guidance document (USEPA, 2002a) states that the index chemical should be selected based on the availability of high quality dose-response data, preferably in each route of interest, for the common mechanism endpoint and that it acts toxicologically similar to other members of the common mechanism group. High quality dose-response data allows the calculation of PoDs for oral, dermal, and inhalation exposures with confidence. Because the PoDs for the index chemical are used to extrapolate risk to the exposure levels anticipated in the human population, any error or uncertainty in an index chemical's PoD value will be carried forward in the cumulative risk estimates.

a. Candidates for the Index Chemical

When selecting the index chemical, EPA evaluated the availability of quality oral, dermal, and inhalation studies for all ten NMCs. Dermal toxicity studies that provided RBC and whole brain data were available for 4/10 NMCs (carbaryl, methiocarb, oxamyl, propoxur). Inhalation studies were available for only propoxur and oxamyl. At present time, the only NMCs with studies in all three routes of interest are oxamyl and propoxur. As shown in Table I.B-2, the oxamyl database of oral studies is more robust than propoxur. Moreover, the oxamyl dermal study in rabbits provides more robust dose-response data compared to the propoxur rabbit dermal study (Tables 1.B-4 and 1.B-7). Consequently, oxamyl has been selected as the index chemical for the revised cumulative risk assessment of the NMCs.

b. Description of the Oxamyl Database

Oxamyl has a robust oral database that includes 6 acute oral studies (4 registration, 1 NHEERL, 1 human). Radiometric ChE data are available from EPA's NHEERL dose-response and time course studies. A comparative



cholinesterase study with juvenile (PND 11) and adult rats is also available (46615301). Doses in oral rat studies ranged from 0.005 to 15.3 mg/kg and thus provide a broad dose-response range. RBC ChE was measured at the time of peak effect in all six studies. Whole (or half) brain ChE data at peak inhibition are available from the five rodent studies. High quality ChE recovery data in adults and PND11 rats are also available. As shown in Table I.B-3, the brain BMD_{10s} for male and female rats are similar. For both sexes, the confidence limits on the BMD_{10s} also are narrow. Thus, the BMDL_{10s} provide robust values for extrapolating cumulative risk.

A double-blind, ascending, single oral dose, human study is also available for oxamyl (MRID 44912301). Multiple RBC ChE sampling events provided the progression of ChE inhibition, maximum inhibition, as well as enzyme recovery for each volunteer. The human study was examined by the HSRB in April 2006 and deemed scientifically robust and ethically sound for use in risk assessment (HSRB Final Report, June 2006).

Two dermal studies were available for oxamyl, both in the rabbit. Oxamyl exhibited a robust dose-response relationship for assessing cholinesterase activity with RBC and brain. The effect of sex on dose was not significant in either study or compartment. RBC and brain (half-brain) ChE activities for both studies were measured once, at the end of the study. The dermal brain and RBC ChE BMD_{10s} are 34.91 and 64.01 mg/kg, respectively.

An acute (single day, 4 hours) inhalation toxicology study (MRID 45155801) is available for oxamyl. Brain and RBC ChE inhibition were measured at the end of the study. The BMD analyses indicate a robust dose-response relationship for assessing ChE activity with RBC and brain. ChE inhibition was similar for both RBC and brain compartments in both sexes. The inhalation brain and RBC ChE BMD_{10s} are 0.005 mg/L and 0.002 mg/L, respectively.

A detailed description of the benchmark dose analysis for dermal and inhalation studies in oxamyl can be found in Appendix II.B.2. Table I.B-7 provides the brain BMD_{10s} and BMDL_{10s} for oxamyl. As the index chemical, it is used to calculate RPFs and PoDs:

- ☐ Oxamyl brain **BMD_{10s}** for oral, dermal, and inhalation routes have been used to calculate the oral, dermal, and inhalation *RPFs* for the revised cumulative risk assessment.
- ☐ Oxamyl brain **BMDL_{10s}** for oral, dermal, and inhalation routes have been used as the oral, dermal, and inhalation *PoDs* in the revised cumulative risk assessment.



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Oral, dermal, and inhalation brain BMD₁₀s and BMDL₁₀s for oxamyl, the index chemical

Endpoint	Oral	Dermal	Inhalation
BMD ₁₀	0.24 mg/kg	34.91 mg/kg	0.0047 mg/L
BMDL ₁₀	0.18 mg/kg	17.05 mg/kg	0.0038 mg/L (converted to 0.66 mg/kg)

6. Relative Potency Factors for the Revised Cumulative Risk Assessment of the *N*-Methyl Carbamates

RPFs were calculated from endpoints for brain ChE inhibition provided in Tables 1.B-3, 1.B-4, 1.B-5, and 1.B-7. An RPF is the ratio of the BMD₁₀ of oxamyl divided by the BMD₁₀ (or appropriate value) for each NMC. RPFs are listed in Table 1.B-8.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Relative potency factors for oral, dermal, and inhalation routes¹

Chemical	Oral RPF	Dermal RPF	Inhalation RPF
Aldicarb	4		
Aldicarb sulfone (Aldoxycarb) ¹	3.44		
Aldicarb sulfoxide ¹	3.68		
Carbaryl	0.15	0.71	0.51
Carbofuran	2.4		
3 & 5-hydroxycarbofuran ²	2.4		
Formetanate HCL	2.18		
Methiocarb	0.18	0.09	0.62
Methomyl	0.67		
Oxamyl	1.00	1.00	1.00
Pirimicarb	0.02		
Propoxur	0.11	0.03	0.18
Thiodicarb	0.89		



¹ Aldicarb sulfone and sulfoxide were not modeled based on metabolite-specific data. Instead they were calculated based on molecular weight conversions from aldicarb assuming equipotent to aldicarb. ² Carbofuran and 3 and 5-hydroxycarbofuran assumed to be equipotent to carbofuran.

7. Intra-species Variability, Inter-species Extrapolation, and FQPA 10X Safety Factors

Typically, EPA applies standard 10X factors to account for inter-species extrapolation and intra-species variability. The FQPA (1996) also mandates that a 10X safety factor be applied to protect for infants and children unless there is sufficient data to support removal of the 10X. For the revised NMC CRA, *the standard 10X intra-species factor is applied to each of the ten N-methyl carbamates*. The inter-species and FQPA 10X factors applied in the NMC CRA are described below.

a. Inter-species Extrapolation Factor in the revised NMC CRA

The rat provides the basis for the RPFs and PoDs in the cumulative risk assessment for the NMCs. As such, a consideration of inter-species extrapolation is necessary (i.e., animal to human). EPA typically applies a 10X factor to account for differences in animals and humans. In the revised NMC CRA, the Agency has retained the 10X inter-species factor for those seven NMCs with no reliable human cholinesterase data. Oral studies with adult human subjects with measurements of peak RBC ChE inhibition and recovery data are available for aldicarb (MRID 42373001), methomyl (MRID 44721401), and oxamyl (MRID 44912301) and provide the basis for refinement of the inter-species factor for these specific NMCs. These three human studies were evaluated by the HSRB in April, 2006 (HSRB Final Report, June 2006). The Board concluded the human intentional dosing studies were ethical and scientifically robust and appropriate for use by the Agency for purposes of risk assessment. It is noted that the carbofuran human oral study was presented to the HSRB in May 2006; however, the Board concluded that it was not scientifically robust and not useful for risk assessment (HSRB Final Report, July 2006). The revised NMC CRA does not include ChE data from the carbofuran human study. For the acceptable human studies, the RBC ChE data were modeled in a consistent fashion with the rat data to calculate human RBC BMD_{10s} and BMDL_{10s}. The Agency then used the RBC BMD₁₀ ratios for rats and humans for the pesticide-specific inter-species factor. A comparison of RBC ChE BMD_{10s} and half-life estimates suggests humans are approximately 2-5 times more sensitive than rats with half-life estimates similar between rats and humans (1-2 hours). The oral BMD_{10s} and BMDL_{10s} generated from the rat and human ChE data for aldicarb, methomyl, and oxamyl along with the corresponding inter-species factors are provided below in Table I.B-9.



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Inter-species uncertainty factors and corresponding rat and human BMD₁₀s and BMDL₁₀s

Chemical	Rat						Human			Inter-species UF
	Brain			RBC			RBC			
	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	½ life (hrs)	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	½ life (hrs)	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	½ life (hrs)	
Aldicarb	F=0.048 M=0.056	F=0.035 M=0.035	1.5	0.031	0.020	1.1	0.016	0.013	1.7	2X
Methomyl	0.486	0.331	1.0	0.204	0.112	0.8	0.040	0.028	1.6	5X
Oxamyl	F=0.145 M=0.185	F=0.111 M=0.143	0.9	0.278	0.158	0.8	0.083	0.068	2.4	3X

BMD estimates are presented as a single estimate when there are no differences between sexes.
Human RBC data obtained from MRID 42373001 (aldicarb), MRID 44721401 (methomyl), MRID 44912301 (oxamyl).
Rat brain and RBC ChE data obtained for aldicarb from MRIDs 43442302, 43442305, 43829601, 43829602, 45068601; for methomyl from MRIDs 44472001, 44487501, 46646401, Padilla et al. 2007; and for oxamyl from MRIDs 44254401, 44472001, Padilla et al. 2007.

b. FQPA Safety Factor

i. Background

The FQPA (1996) instructs EPA, in making its “reasonable certainty of no harm” finding, that in “the case of threshold effects, **an additional tenfold margin of safety** for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account **potential pre- and post-natal toxicity and completeness of data with respect to exposure and toxicity to infants and children.**” Section 408 (b)(2)(C) further states that “the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children.”

The FQPA requires that the Agency consider issues related to toxicity and exposure. The text contained in this chapter only considers potential sensitivity of infants and children with respect to toxicity. The risk characterization chapter (I.G) contains a more complete discussion of issues related to exposures from food, water, and in/around the home that could contribute to increased exposure to infants and children relative to adults. However, the Agency believes that there are quality data and scientifically supportable methods to account for specific exposure and behavioral patterns of children. Because characteristics of children are directly accounted for in the exposure assessment and the Agency’s methods are not expected to underestimate exposure to NMCs, evaluating the potential for increased toxicity of juveniles is



the key component in determining the magnitude of the FQPA factors in the revised NMC CRA.

As described in detail in OPP's cumulative risk assessment guidance, determination of relative toxic potency should be calculated using a uniform basis of comparison, by using, to the extent possible, a common response derived from the comparable measurement methodology, species, and sex for all the exposure routes of interest (USEPA 2001a, 2002a). For the NMCs, estimates of relative potency are required for 10 pesticides. Toxicology studies in the adult rat provide the most extensive cholinesterase activity data for all routes, compartments, and both sexes and as a result provide the basis for the RPFs and PoDs in the NMC CRA. Since adult rat data have been used to derive the RPFs and PoDs, EPA has retained the 10X FQPA safety factor unless reliable data are available addressing the sensitivity of the young such that EPA can determine that a different safety factor value is protective of infants and children. Consistent with the mode of action for NMCs (i.e., neurotoxicity mediated through the inhibition of AChE via carbamylation of the active site), the comparative cholinesterase assays in juvenile and adults provide the most relevant data for evaluating potential sensitivity to infants and children to NMCs.

The Agency has compared the sensitivity of NOAELs (No-Observable-Adverse-Effect-Level), LOAELs (Lowest-Observable-Adverse-Effect-Level), and BMDs from developmental neurotoxicity studies (DNTs) and comparative cholinesterase studies for OPs as well as NMCs. The Agency has three developmental neurotoxicity studies for the NMCs (aldicarb, carbaryl and carbofuran). For every OP and NMC evaluated, the comparative cholinesterase assays (CCA) provide a more sensitive (i.e., lower) endpoint than the respective DNT. In the case of NMCs, the CCA studies are 10-100 fold more sensitive than the DNT studies. Thus, use of AChE inhibition as the endpoint for evaluating the FQPA 10X safety factor is expected to be protective of functional and behavioral effects.

The Agency has focused its evaluation of the FQPA 10X safety factor on post-natal exposure to juvenile rats. In a detailed analysis provided in the OP CRA (USEPA 2006), the Agency showed that following *in utero* exposure to OPs, dams exhibit larger amounts of ChE inhibition compared to fetuses. In other words, protecting against inhibition in the pregnant dams is believed to protect against pup AChE inhibition *in utero*. In contrast to this *in utero* exposure, pups have been shown to be more sensitive than adults in post-natal studies. Thus, data from post-natal exposures in juvenile and adult rats provide the most robust toxicity data for determining the magnitude of the FQPA safety factor for the NMC CRA. The CCA studies provide sensitive and reliable results, and have been identified for use in the cumulative risk assessment as the most appropriate studies for developing the chemical-specific factor to address the potential susceptibility of infants and children to the effects of NMC



exposure. Comparative ChE data are available and can be used to derive a chemical-specific factor for use in the cumulative risk assessment to reflect the differential sensitivity of children and infants compared to adults. For those NMCs without such data, the FQPA 10X safety factor is retained.

As described in detail below, the Agency has used a dose response modeling approach for evaluating quantitatively the relative sensitivity between juvenile and adult rats. In this approach, a BMD was calculated for juvenile and adult brain ChE data. The ratio of the juvenile and adult BMDs from the specific CCA study was calculated—this ratio has been used mathematically as the data-derived, chemical-specific FQPA safety factor. This approach is similar to that used in the OP CRA but different from (although not inconsistent with) approaches used in the single chemical aggregate risk assessments. In single chemical, aggregate risk assessments, the mathematical calculations are more simple and straightforward as only one active ingredient is included. As such, in single chemical risk assessments, when available, data from young or juvenile animals can be (and have been) used directly as the PoD. When the data from the young are used directly in deriving a PoD and the PoD is established based on the most sensitive effects, the FQPA safety factor can be reduced or removed so long as there are no residual concerns regarding potential pre- and post-natal toxicity or concerns regarding the completeness of the toxicity or exposure databases. In the revised NMC CRA, the data-derived FQPA safety factor is used to adjust the chemical specific RPF to account for the potential increased sensitivity of the young.

The Agency has relied primarily on CCA studies in juvenile and adult animals to evaluate the potential sensitivity of young animals to cholinesterase inhibition. Brain cholinesterase inhibition is the focus of this analysis as brain cholinesterase inhibition has been selected as the endpoint for derivation for RPFs and PoDs in the NMC CRA. For each individual NMC, the magnitude of the FQPA 10X safety factor was based on the ChE dose-response data comparing relative sensitivity of adult and juvenile animals. The Agency has also evaluated the recovery data in the young to evaluate the extent to which the young recover from NMC inhibition in comparison to adults (e.g., faster, slower, or similar to adults). If the Agency were to evaluate NMC exposure at shorter intervals than 24 hours (Chapter C), then the Agency would need to account for the half-life to recovery in young animals. The Agency has four CCA studies generated by registrants: carbofuran, formetanate, methomyl, and oxamyl. In addition, NHEERL has provided comparative sensitivity data for aldicarb and carbaryl. The brain BMD₁₀ estimates for PND 11 pups span an order of magnitude and are generally 2-3 times lower than adult rats. The half-life estimates for brain inhibition in PND11 rats range from approximately 30 minutes to almost 10 hours compared to 1 to 4 hours in adults. Table I.B-10 displays the BMD₁₀ values of both juvenile (PND11 or PND17) and adult rats specifically from the available CCA studies. It is noted that the adult BMD₁₀ estimates from the CCA study may be different than the more robust BMD₁₀



estimate based on the combined adult data. BMDL₁₀ and half-life values for pups are provided for information purposes only.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Dose-response and recovery half-life estimates in juvenile and adult rats from comparative cholinesterase studies

Chemical	PND11 Brain			Adult Brain
	BMD ₁₀ (mg/kg)	BMDL ₁₀ (mg/kg)	Half-Life (hrs.)	Adult BMD (mg/kg)
Aldicarb ¹	0.017	0.016	NA ²	0.033
Carbaryl	1.459	1.135	5.4 ³	2.627
Carbofuran	0.039	0.030	3.0	0.109
Formetanate	0.188	0.098	9.5	0.382
Methomyl	0.104	0.070	0.4	0.317
Oxamyl	0.051	0.025	1.5	0.177.

¹The juvenile rat data for aldicarb is based on a published acute oral neurotoxicity study in PND17 rats (MRID45068601), ²Time-course data in juvenile rats not available for aldicarb; ³The recovery half-life estimate for carbaryl is based on NHEERL data from PND17 pups.

The resulting FQPA safety factor for each NMC is the ratio of the BMD₁₀ for adult/pup. Those NMCs without comparative cholinesterase data retain the 10X FQPA safety factor. Since the FQPA safety factor is specific to protecting children and developed from juvenile rat data, it may be applied in the NMC CRA to scenarios specific to children's exposure. The FQPA safety factor is therefore not applied to RPFs for adults. The resulting chemical specific FQPA safety factors for these six NMCs are listed in [REF _Ref177880446 \h].

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. FQPA safety factors for the revised NMC CRA¹

Chemical	FQPA Safety Factor
Aldicarb	2.0
Carbaryl	1.8
Carbofuran	2.75
Formetanate	2.03
Methomyl	3.05
Methiocarb	10
Oxamyl	3.48
Pirimicarb	10
Propoxur	10
Thiodicarb	10

¹Those NMCs without juvenile pup data retain the 10X FQPA safety factor



8. Incorporation of Uncertainty/Extrapolation Factors and the Target Margin of Exposure

In general, when performing a cumulative risk assessment using a RPF approach, like that done for the NMCs, uncertainty and extrapolation factors can be incorporated into the risk assessment in two different ways: 1) adjustment of the chemical-specific RPF or 2) incorporation into the target Margin of Exposure. Both ways are used in the NMC CRA.

Adjustment of the Chemical Specific RPF: In cases where the uncertainty or extrapolation factor varies among the chemicals, the chemical-specific RPF is adjusted (i.e., multiplied) by the uncertainty or extrapolation factor. In the case of the NMCs, the FQPA and inter-species factors vary among the chemicals. As such, the Agency has multiplied the FQPA safety and inter-species factors by the RPFs to generate adjusted RPFs for each NMC ([REF _Ref177880446 \h]).

Incorporation into the Target Margin of Exposure (MOE): There may be assessments where the magnitude of an uncertainty or extrapolation factor is the same for each member of the common mechanism group. In these assessments, the target MOE identified addresses the total magnitude of the uncertainty or extrapolation factor(s). This is the situation for the intra-species factor in the NMC CRA where the standard 10-fold factor has been applied. As discussed above, both the FQPA safety and inter-species extrapolation factors are accounted for in the adjusted RPFs for the NMC CRA. As such, the target MOE for the NMC CRA is 10 accounting for intra-species variability.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Adjusted oral relative potency factors for children and adults based on inter-species and FQPA specific factors

Chemical	Oral RPF	Inter-species Factor	FQPA Factor Children Only	Adjusted RPF Children	Adjusted RPF Adult
Aldicarb	4	2	2	16	8
Aldicarb sulfone (Aldoxycarb)	3.44	2	2	13.8	6.9
Aldicarb sulfoxide	3.68	2	2	14.7	7.4
Carbaryl	0.15	10	1.8	2.7	1.5
Carbofuran	2.4	10	2.75	66	24
5-hydroxycarbofuran	2.4	10	2.75	66	24
Formetanate HCL	2.18	10	2.03	44	22
Methiocarb	0.18	10	10	18	1.8
Methomyl	0.67	5	3.05	10	3.3
Oxamyl	1	3	3.48	10	3
Pirimicarb	0.02	10	10	2	0.2
Propoxur	0.11	10	10	11	1.1
Thiodicarb	0.89	10	10	89	8.9



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Adjusted dermal relative potency factors for children and adults based on inter-species and FQPA specific factors

Chemical	Dermal RPF	Inter-species Factor	FQPA Factor Children Only	Adjusted RPF Children	Adjusted RPF Adults
Carbaryl	0.71	10	1.8	13	7.1
Methiocarb	0.09	10	10	9	0.9
Oxamyl	1.00	3	3.48	10	3
Propoxur	0.03	10	10	3	0.3

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Adjusted inhalation relative potency factors for children and adults based on inter-species and FQPA specific factors

Chemical	Inhalation RPF	Inter-species Factor	FQPA Factor Children Only	Adjusted RPF Children	Adjusted RPF Adults
Carbaryl	0.511	10	1.8	9	5.1
Methiocarb	0.619	10	10	62	6.2
Oxamyl	1.00	3	3.48	10	3
Propoxur	0.178	10	10	18	1.8

9. Dose Additivity

A key assumption of the RPF method is dose additivity. While there are a few interaction studies of *N*-methyl carbamate and OP pesticides in the literature (e.g., Gupta and Dettbarn, 1993; Takahashi *et al.*, 1987), no studies conducted using mixtures of more than two *N*-methyl carbamates and which use low dose levels (i.e., that do not produce lethality or profound toxicity) have been identified. To fill this data need, NHEERL scientists have conducted a mixture study using seven *N*-methyl carbamates (carbaryl, carbofuran, formetanate HCl, methiocarb, methomyl, oxamyl, and propoxur) (Padilla *et al.*, 2006). In the mixture study, a dose-additive experimental design was used and the proportion of the carbamates in the mixture was based on their potency using the individual-chemical benchmark dose values as the point of comparison. Five different dosage levels of the mixture were given, predicted to produce <5%, 10%, 25%, 45% or 60% brain ChE inhibition. Each NMC was given alone at a previously tested dosage to confirm the original dose-response data (7 single-chemical experimental groups). The effects on motor activity and RBC and brain ChE were measured. As can be seen from [REF _Ref177881426 \h] below, increasing dosages of the mixture produced increasing decrements in brain ChE activity. Moreover, the dose-additive model predicted the degree of ChE inhibition within the 95% confidence limits of each predicted value. Additivity was also measured in the RBC ChE and motor activity evaluations (manuscript in preparation).



Figure I.[STYLEREF 2 \s]-[SEQ Figure * ARABIC \s 2]. Plot of brain ChE measured in a seven chemical mixture of *N*-methyl carbamates

10. Summary

This chapter has described the application of the RPF method in the revised cumulative hazard assessment for the NMCs. Whole brain ChE is a sensitive, health protective endpoint representing the target tissue. The brain data provide the most appropriate dataset for extrapolating cumulative risk to this common mechanism group. Potency for the NMCs varies over several orders of magnitude. Analysis of recovery data for brain ChE in adults suggests that half-life time to recovery ranges from less than an hour up to 4 hours is chemical dependant, and for some chemicals, is dose dependant. For some NMCs, recovery of ChE activity in pups may be longer. Overall, the analysis of recovery data supports the Agency's assumption that at the low concentrations found in the environment, the appropriate duration of exposure for the NMC cumulative risk assessment is acute exposure. Oxamyl has been selected as the index chemical based on the availability of high quality dose response data for the oral, dermal, and inhalation routes. BMDL₁₀ estimates of brain ChE from oral, dermal, and inhalation studies with oxamyl represent the PoDs for the NMCs cumulative risk assessment. BMD₁₀ estimates of brain ChE from oral, dermal, and inhalation studies were used to develop RPFs for the NMCs.



The Agency has, when available, utilized ethically and scientifically valid human studies for refinement of the inter-species factor as well as comparative sensitivity rat data for refinement of the FQPA safety factor. These uncertainty factors apply to the oral, dermal, and inhalation RPFs, which result in adjusted RPFs for individual NMCs, specifically for adults and children. In instances where there is no human study or comparative sensitivity data for particular NMCs, the inter-species factor and/or FQPA safety factor remain(s) unchanged (i.e., 10x) and is/are used to adjust the RPF accordingly. As a result, the target MOE for the NMC CRA is 10 which accounts for the intra-species 10x factor which is the same for all of the NMCs in the revised NMC CRA.



C. Cumulative Risk from Pesticides in Foods

This chapter discusses the cumulative risk associated with the food exposure pathway. As with previous cumulative assessments released by OPP, the data for this pathway are developed from two primary sources: dietary consumption data collected by USDA's Continuing Survey of Food Intakes by Individuals (CSFII) and pesticide residue monitoring data collected by the USDA Pesticide Data Program (PDP). As described further in Chapter I.B of this document, oxamyl serves as the index chemical and the residue values for the other NMC pesticides were converted to oxamyl equivalents using the RPF approach. The exposure estimates presented in this chapter, therefore, are expressed in terms of the index chemical oxamyl.

The purpose of this chapter is several-fold: (i) to describe and characterize the food consumption, pesticide residue, and other data sources used to develop the cumulative risk assessment for the food pathway; (ii) to describe how and the extent to which the PDP pesticide residue data on approximately 80 food commodities, including those most commonly consumed by children, was extended/translated to other foods in order to produce a more complete data set on pesticide residues that more nearly approximated the total diet; (iii) to describe the methods used to convert pesticide residue data from the PDP data program into index-chemical (i.e., oxamyl) equivalents in order to conduct a cumulative assessment; (iv) to describe how this cumulative residue data set was combined with USDA's food consumption data and food processing data to produce a distribution of estimated cumulative exposures to the NMC group of pesticides; and (v) to provide information with respect to those crop-commodity combinations which contribute to exposure at the upper-ends of the exposure distribution. This chapter does not describe the extensive sensitivity analyses that were performed nor does it provide information on or discuss risk characterization. These are important -- indeed critical -- components of any risk assessment and are presented in Chapter G of this document.

1. Food Consumption Data

Data on food consumption are a necessary component for estimating pesticide exposure through the diet. For the revised NMC CRA, food consumption data were obtained from the USDA CSFII 1994-96/1998 (USDA, 2007). The CSFII 1998 incorporated a supplemental children's survey conducted in 1998 in which the food consumption of an additional 5,559 children (birth through 9 years old) were surveyed. The CSFII 1994-96/1998 is a nationally representative stratified, multi-stage area probability sample with a target population consisting of non-



institutionalized individuals in all 50 states and Washington, DC. CSFII 1994-96/1998 data are derived from information provided by 20,607 individuals who participated in the survey. Individuals who took part in the survey were asked to provide two non-consecutive days of dietary data through the administration of in-person, 24-hour dietary recalls spaced 3–10 days apart. The USDA CSFII consumption survey data are included as an integral component of the DEEM-FCID™ software used to conduct this cumulative risk assessment.¹

As in previous cumulative risk assessments produced by EPA, separate assessments were conducted on the various sub-populations as represented in the CSFII 1994-96/1998. The current assessment reports on the U.S. general population and the following standard age groups:

- ☐ Infants less than 1 year old
- ☐ Children 1-2 years old
- ☐ Children 3-5 years old
- ☐ Children 6-12 years old
- ☐ Youths 13-19 years old
- ☐ Adults 20-49 years old
- ☐ Adults 50+ years old
- ☐ Females 13-49 years old

¹ It is important to note that the CSFII food diary information is expressed in terms of food as *consumed* (e.g., pizza, apple pie, lasagna, etc.) while OPP's assessments are currently conducted in terms of food *commodities* (e.g., tomatoes, milk, wheat flour, beef, apples, etc.). OPP uses standard recipes to convert foods "as consumed" as reported in CSFII diaries into food commodities for use in OPP dietary risk assessments. The recipe information used to break down the foods was developed jointly by EPA and USDA and is one module in the EPA's Food Commodity Intake (FCID) database which is available upon request. Thus, while this NMC CRA refers to "food" consumption from CSFII, the Agency's calculations are performed in functionally equivalent "food commodity" terms from FCID. While often distinct, "food" and "food commodity" will be used interchangeably in this document.



2. Pesticide Residue Data

There are multiple sources of pesticide residue data (on food) available to EPA. However the sampling design and extent, intent, and representativeness of these various sources of pesticide residue data differ. USDA PDP provides the most comprehensive sampling design, and the most extensive and intensive sampling procedures for pesticide residues of the various data sources available to EPA. Additionally, the intent of PDP's sampling design is to provide statistically representative samples of food commodities eaten by the U.S. population specifically for the purpose of performing dietary risk assessments for pesticides. As such, PDP serves as the only source of pesticide residue data used in quantitative manner in the dietary portion of this revised NMC CRA. The other sources of pesticide residue data are used in a qualitative manner to ensure that EPA is not significantly underestimating pesticide exposure through food. The various sources of pesticide residue data are discussed below.

a. USDA-PDP

As with the preliminary NMC CRA, this revised NMC CRA also relies exclusively on the PDP program for residue data that are used quantitatively. The USDA PDP is a cooperative effort by federal and state agencies to obtain statistically-reliable data on pesticide residues in food (USDA, 2007a). Federal funds support sampling, testing, and data-reporting activities conducted by participating states. The participating states include California, Colorado, Florida, Maryland, Michigan, Minnesota, Montana, New York, Ohio, Texas, Washington, and Wisconsin. In addition, 13 of their neighboring states are in the direct distribution networks of the PDP participating states. Together, these states represent over 50% of the nation's population and all 4 census regions of the U.S. These states also represent the major commercial production areas of fruit and vegetables in the U.S.

The PDP sample collection procedures are specifically designed to produce dietary exposure estimates that closely approximate real world exposures. Samples are collected by USDA at terminal markets and warehouses immediately before these commodities are shipped to supermarkets and other retail establishments. Both domestically produced and imported foods are subject to sampling. Sampling is conducted in accordance with a statistically-based plan designed and put in place by USDA's National Agricultural Statistics Service (NASS) to be representative of the U.S. food supply. Samples are prepared by the analytical laboratory as if for consumption (i.e., they are washed, peeled, and/or cored, as appropriate) and thus are more reflective of actual exposures than data typically available from field trials or FDA monitoring



programs. Thus, measurements simulate as closely as possible dinner-plate exposures to consumers.

The program focuses on high-consumption foods for children and reflects foods typically available throughout the year. A complete description of the PDP program and all data through 2005² are available online (USDA, 2007b). The PDP data are available in downloadable electronic format from this site and can be easily transferred, imported, analyzed, and summarized. Appendix [REF _Ref178095643 \r \h] lists all of the FCID food commodities for which PDP residue data were used to estimate dietary exposure to NMC pesticides. The PDP residue data on NMC pesticides included in the revised NMC CRA are summarized in Appendix [REF _Ref178095665 \r \h * MERGEFORMAT].

b. NMC Market Basket Survey

The Carbamate Market Basket Survey Task Force sponsored a market basket survey (MBS) of NMC pesticide residues and their toxicologically relevant metabolites in single-serving samples of fresh fruits and vegetables collected in 1999-2000 (Carringer, 2000). The NMC pesticides analyzed in the MBS were aldicarb, carbaryl, carbofuran, methomyl, oxamyl, and thiodicarb. The food commodities sampled in the MBS were apple, banana, broccoli, grape, head lettuce, orange, peach, and tomato. However, not all NMC pesticides were analyzed in each type of commodity. For instance, aldicarb was analyzed in only one commodity, oranges; and carbaryl was the only NMC analyzed in all eight food commodities. Of the top ten pesticide-commodity combinations contributing to the exposure of young children as determined by this NMC CRA, only two (for children 1-2) and three (for children 3-5) of these significant contributors were sampled in the MBS. Comparing the residue data from the PDP program with the MBS, the top pesticide-commodity contributors common to both MBS and PDP have similar ranges of pesticide concentrations and frequencies of detects. Additionally, PDP has collected more recent data on the same commodities sampled in the MBS. Finally, all of the pesticide-commodity combinations analyzed in the MBS are data for which EPA already has adequate PDP data for the purpose of dietary risk assessment. Consequently, the MBS data have not been used directly in the revised NMC CRA.

² Although the 2006 PDP data are not currently available for download from the PDP website, the new data are expected to be published and publicly available in 2007. Due to an active interagency MOU between USDA PDP and USEPA OPP, the 2006 PDP data on NMC pesticides were given priority in PDP's QA/QC process and released early to OPP upon request.



c. FDA-CFSAN Pesticide Residue Monitoring Program

The Food and Drug Administration's (FDA's) Center for Food Safety and Applied Nutrition (CFSAN) Pesticide Residue Monitoring Program is designed primarily for enforcement of EPA pesticide tolerances on imported foods and domestic foods shipped in interstate commerce (USFDA, 2007a). In this monitoring program, domestic samples are generally collected close to the point of production in the distribution system. Import samples are collected at the point of entry into U.S. commerce. The emphasis in sample collection is on the agricultural commodity which is analyzed as the unwashed, whole (unpeeled), raw commodity. Processed foods are also included in the program. Because the emphasis of this program is not on dietary exposure, it is being used in the current assessment mostly as a semi-quantitative check on the potential for residues and as support for data from other sources. The program has extensive data available on eggs and fish, which support the judgment that NMC residues are negligible on these foods as consumed. Thus, the FDA data were used in a qualitative manner in this revised NMC CRA to support the decision to assign residue values of zero to the NMC residues on eggs and fish effectively removing these food commodities from the assessment. Appendix II.C.1 indicates the foods for which such decisions were supported by this program.

d. FDA-CFSAN Total Diet Study

The FDA's CFSAN Total Diet Study (TDS) has provided data on concentrations of contaminants in a wide range of foods for about 46 years (USFDA, 2007b). Foods are purchased at retail (from grocery stores and fast-food restaurants), generally 4 times a year, prepared and cooked for consumption, and analyzed by highly sensitive multi-residue methods. Between 1991 and 2004, there have been 48 market baskets collected. For each market basket, three samples of approximately 280 different foods are collected and composited, and the composite samples are analyzed for – among other things – NMC pesticide residues. A disadvantage of these data is that only one composite sample of each food is analyzed in each market basket. For this reason, these data have been used primarily as semi-quantitative support for judgments on residues in foods.

In previous cumulative risk assessments performed by EPA, conservative estimates of pesticide residue values for some highly consumed foods such as beef were based on the TDS data. However, beef, poultry, and pork are now sampled under the PDP program, being most recently sampled in 2002, 2005, and 2006, respectively. PDP data on these commodities serve as the primary source of residues of



pesticides used by EPA in dietary risk assessments, replacing the corresponding FDA TDS data previously used. Both programs have found very few detects of low concentration NMC residues in these commodities supporting the previous understanding that beef, poultry, and pork are negligible contributors to dietary exposures to the NMC pesticides. The TDS data also includes samples of fish and eggs. The analytical results for these samples confirm those of the FDA surveillance monitoring program, namely, that fish and eggs contain negligible concentrations of NMC pesticides.

3. NMC Pesticides Included in the Food Risk Assessment

The *N*-methyl carbamate Cumulative Assessment Group (CAG) consists of 10 NMC pesticides. These 10 pesticides (along with their ChE—inhibiting metabolites and their associated RPFs) are listed in [REF _Ref178481623 \h].

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. *N*-methyl Carbamates^a and RPFs

Chemical	RPF (Oral)
Carbaryl ^b	0.15
Aldicarb	4
Aldicarb sulfone (Aldoxycarb)	3.44
Aldicarb sulfoxide	3.68
Oxamyl (Index Chemical) ^b	1
Formetanate hydrochloride	2.18
Methomyl	0.67
Carbofuran	2.4
3-Hydroxycarbofuran	
Propoxur	0.11
Methiocarb	0.18
Thiodicarb	0.89
Pirimicarb	0.02



^a See "Carbamate Cumulative Assessment Group: Availability" (USEPA, 2004a).

^b The carbaryl metabolite, 1-naphthol and the oxamyl metabolite, oxamyl oxime were analyzed by PDP, but not included in the dietary assessment since these compounds are not known to inhibit acetylcholinesterase.

The above listed pesticides and metabolites were used as a "starting point" in determining which pesticides (and associated metabolites) would be considered in the food pathway of the NMC CRA. During the period since the issuance of the preliminary NMC CRA in August 2005, the Agency identified, and in some cases imposed, risk reduction measures on some of the major contributors to carbamate cumulative risk. The risk estimates presented in this revised NMC CRA reflect the risk mitigation measures identified for or taken on individual carbamates since FQPA was signed into law in August 1996. These mitigation measures generally reflect determinations of risk based on the single-chemical risk assessments. For all of the risk mitigation measures that are reflected in this document, EPA has either commenced the processes necessary to implement its selected risk mitigation or intends to commence the appropriate processes in the near future. Having already determined that the identified risk mitigations are warranted for the individual chemicals regardless of the cumulative assessment, EPA has chosen to reflect that mitigation in this assessment. Consequently pesticide-crop combinations that have been (or are being) cancelled or not considered eligible for reregistration³, do not have food uses, or have had significant and substantial label modifications were excluded from the 1994 to 2006 PDP residue data. As a practical matter, EPA determined that it would serve no purpose to include such uses in the cumulative assessment. Other than by adding a new issue that might delay action, adding these uses would not likely have any impact on the timing or substance of any cancellation decision relating to such uses. And given that the purpose of tolerance reassessment is to determine whether regulatory action should be initiated to modify or revoke tolerances that the Agency finds do not meet the safety standard of section 408, there seems to be little value in including uses in the assessment that will disappear regardless of their impact on cumulative risk. The critical issue for determining whether regulatory action will have to be initiated under section 408 is whether the uses that will remain result in unacceptable dietary risk. EPA recognizes, however,

³ Although residues resulting from uses that no longer exist were removed from this revised NMC CRA, EPA continues to incorporate violative residues in its cumulative risk assessments to reflect potential exposure to residue not consistent with registered label uses. These violative residues represent pesticide concentrations in PDP samples either above an already existing tolerance level (possibly due to agricultural practices not consistent with label instructions) or in a commodity for which no tolerance has been established.



that to the extent that any risk mitigation measures are not subsequently implemented as envisioned in this revised NMC CRA, the cumulative assessment will have to be revised as necessary.

Table in Appendix [REF_Ref178097308 \r \h] provides a summary of the PDP samples including the total number of laboratory analyses completed for the NMC pesticides and metabolites on each food commodity in the database. PDP analytical data for the above pesticides (and their associated metabolites⁴, where applicable) are being used in the NMC CRA assessment for the food pathway. Additional details regarding these pesticides and their inclusion in the assessment NMC CRA food pathway assessment are provided below.

Aldicarb: Aldicarb or its sulfoxide and/or sulfone metabolites have been detected in more than 1% of the PDP samples of the following commodities: potato, sweet potato, grapefruit, and orange juice. It has been detected in less than 1% of the samples of the following commodities: green bean, cantaloupe, grape, orange, sweet corn, and poultry liver. PDP reports each of these compounds (all of which are acetylcholinesterase inhibitors) in terms of the parent or specific metabolite *per se*. The metabolites have higher molecular weights than the parent, but the RPF for aldicarb is based on the concentration of the parent chemical. Therefore, the metabolite RPFs were adjusted to account for the higher molecular weight of the metabolites compared to the parent chemical. The conversion of the metabolite concentrations to parent concentrations is important since the majority of detectable aldicarb residues found in PDP commodities are the metabolites.

Carbaryl: Carbaryl has been detected in more than 1% of the PDP samples of the following commodities: apple, apple juice, apple sauce, peach, strawberry, pear, pear juice, grape, grape juice, green bean, orange, nectarine, cantaloupe, carrot, celery, cherry, cranberry, cucumbers, eggplant, grapefruit, orange, orange juice, pineapple, plum, prune, pork fat, pork meat, chicken meat, raisin, rice, spinach, sweet bell pepper, sweet pea, tomato (canned), and asparagus. It has been detected in less than 1% of the samples of the following commodities: banana, broccoli, cauliflower, heavy cream, lettuce, milk, sweet potato, tomato (fresh), watermelon, wheat, and winter squash. Significant label changes, primarily lengthened pre-harvest intervals and reduced application rates, occurred for apple, peach, and strawberry in the late 1990's (Lantz and Young, 2006). These label changes have resulted in lower residue levels for these three crops making only the 2000 and later PDP data relevant. Thus, for the revised NMC CRA, only PDP data for

⁴ The carbaryl metabolite, 1-naphthol and the oxamyl metabolite, oxamyl oxime, were analyzed by PDP, but not included in the dietary assessment since these compounds are not known to inhibit AChE.



periods during 2000-2006 were used for apple, peach, and strawberry; whereas, the full PDP dataset (1994-2006) was used for all other commodities with carbaryl detects.

Carbofuran: Carbofuran has been detected in more than 1% of the PDP samples of the following commodities: cucumber, kale greens, sweet bell pepper, and wheat. It has been detected in less than 1% of the samples of the following commodities: cantaloupe, grape, grape juice, green bean, spinach, watermelos, and winter squash. EPA has determined that all domestic carbofuran uses are ineligible for reregistration and this chemical is undergoing cancellation (USEPA, 2006e). Thus, the revised NMC CRA includes only carbofuran uses on the following imported commodities for which tolerances are being retained: bananas, rice, sugarcane, and coffee⁵.

Formetanate HCl: Formetanate has been detected in more than 1% of the PDP samples of nectarines and pears. It has been detected in less than 1% of the samples of apples and oranges. Formetanate is analyzed by PDP using a single-residue method and not all PDP commodities have been analyzed using this method. The laboratory performing this analysis ceased participating in the PDP program after 2001. Thus, PDP data are only available for formetanate on orange, pear, nectarine and apple through 2001. Late season uses on oranges, nectarines, and apples were cancelled and field trial data conducted by the registrant using only early-season applications demonstrate that no detectable residues are expected (USEPA, 2006f). Thus, formetanate residues on oranges, nectarines and apples are assumed to be negligible and were not considered in the revised NMC CRA. Only formetanate use on pear has been included in the assessment, and then only using data from 1997 and 1998.

Methiocarb: Methiocarb has been detected in less than 1% of the PDP samples of cauliflower, cherries, cucumbers, and sweet bell peppers. Methiocarb has not been detected on any other PDP commodities.

Methomyl: Methomyl has been detected in more than 1% of the PDP samples of the following commodities: apple, asparagus, broccoli, cantaloupe, cauliflower, celery, cucumbers, eggplant, grape, green bean, kale greens, lettuce, nectarine, peach, spinach, strawberry, summer squash, sweet bell pepper, and watermelon. It has been detected in less than 1% of the samples of the following commodities: carrot, orange, pear, tomato, and winter squash. PDP data for all crops except grape and strawberry were included in the revised NMC CRA. A voluntary cancellation request has been received by the Agency for methomyl use

⁵ Sugarcane and coffee are not assumed to contain residues of carbofuran due to the extensive processing, purification, and refinement to which the commodities are subjected.



on grapes, and the strawberry use was voluntarily canceled by the registrant early in 2007. Thus methomyl residues on grapes and strawberries were not incorporated into the assessment. In an effort to better reflect NMC residues on foods as eaten, the PDP lettuce samples were divided into leaf and head where information regarding the lettuce variety was available. Separating the lettuce varieties ensured that leaf lettuce residues, which tend to be higher than head lettuce residues, were not inappropriately assigned to foods that contain head lettuce as an ingredient, as per the FCID recipe files.

Oxamyl: Oxamyl (parent) has been detected in more than 1% of the PDP samples of the following commodities: cantaloupe, celery, cucumber, eggplant, lettuce, pear, potato, summer squash, sweet bell pepper, tomato and watermelon. It has been detected in less than 1% of the samples of the following commodities: apples, green bean, orange, spinach, and winter squash. An oxamyl metabolite, oxamyl oxime, also detected in the PDP program, was not considered in the assessment since it does not inhibit acetylcholinesterase.

Pirimicarb: Pirimicarb has been detected on less than 1% of the PDP samples of peach and sweet bell pepper. Pirimicarb has not been detected on any other PDP commodities.

Propoxur: Propoxur has not been detected on any PDP commodities.

Thiodicarb: Thiodicarb has been detected on less than 1% of PDP samples of pear. Thiodicarb has not been found on any other PDP commodities.⁶

4. Food Commodities Included in the Food Risk Assessment

The universe of foods included in the cumulative dietary exposure assessment is defined by the USDA CSFII 1994-96/1998. The CSFII food diary information is expressed in terms of food *as consumed* (e.g., pizza, apple pie, lasagna, etc.). These foods as reported in CSFII diaries are converted to food *commodities* (e.g., tomatoes, milk, wheat flour, beef, apples, etc.) using standard recipes. The recipe information used to break down the foods was developed jointly by EPA and USDA and is

⁶ Although the PDP analytical methods usually convert thiodicarb residues to methomyl, the majority of methomyl residues detected in PDP commodities are assumed to be the result of methomyl use rather than thiodicarb use. The basis for this assumption is that the number of registered uses for thiodicarb is much less than those for methomyl and pesticide usage information indicates very low thiodicarb use on food crops for which it is registered. Since methomyl residues resulting in the highest exposures are from food crops for which thiodicarb is not registered, the assumption that all PDP methomyl residues are due to methomyl use (rather than thiodicarb use) is not expected to significantly underestimate dietary exposure to thiodicarb.



one module in the EPA's Food Commodity Intake (FCID) database. Table in Appendix II.C.1 lists all of the FCID food commodities (translated from CSFII foods) in decreasing order of their relative per capita consumption by children 1-2 years old and children 3-5 years old while table in Appendix II.C.5 contains a complete listing of the FCID food commodities *and* food forms (e.g. "Cooked; Fresh or N/S; Cook Meth N/S") in the DEEM-FCID™ software that were included in this assessment. This table also includes summary information on the residue distributions that were prepared from the revised NMC CRA food residue database as input for each food form. The actual DEEM-FCID™ input files and associated residue files will be made available on the internet or upon request via CD-ROM for any interested party.

PDP has an extensive monitoring program that focuses on food commodities commonly consumed by children and includes a variety of fruits, vegetables, meat/poultry/pork products, dairy products, and grains. In all, 80 food commodities monitored by PDP are included in the revised NMC CRA. Food processing factors that reflect reduction or concentration of NMC pesticides in processed foods were applied to food commodities or specific pesticide-commodity pairs in the PDP program to extend these data for use on cooked and processed food/food forms in the analysis. Through the 80 foods commodities directly analyzed by PDP, the revised NMC CRA accounts for approximately 93% of the foods consumed by children 1-2 years of age.

As mentioned previously, the PDP residue data were further extended to other commodities identified as reasonable for translation of pesticide residue data per Agency policy. That is, residue data on commodities which were analyzed by PDP were translated to similar food commodities with registered uses which were not analyzed by PDP. In this way, residues on foods accounting for an additional 1% of the per capita consumption of children 1-2 years of age were estimated using these translated PDP data. For example, cantaloupe melon residues are translated to honeydew melon and peach residues are translated to apricot. Translations were made using HED SOP 99.3 (USEPA, 1999b) as summarized in [REF_Ref177527537 \h * MERGEFORMAT].



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Crop Translations for Pesticide Monitoring Data

Commodity Analyzed	Commodity translated to...	Comments
Potato	Subgroup 1-C	
Carrot	Subgroup 1-A or 1-C	
Head Lettuce	Cabbage, Chinese cabbage Napa (tight headed varieties), Brussels sprouts, radicchio	All have a head morphology best represented by lettuce. All are in Subgroup 5-A except radicchio (4-A).
Broccoli	Cauliflower, Chinese broccoli, Chinese cabbage bok choy, Chinese mustard, kohlrabi	Broccoli better represents these heading, thickly stemmed and/or more branching cole crops than spinach does.
Spinach	Subgroup 4-A, Subgroup 5-B and Subgroup 4-B (except celery and fennel unless a strong case can be made)	Celery and fennel typically are excluded since residues may be higher in these crops due to the whorled, overlapping petioles which may retain spray residues.
Green Bean	Subgroups 6-A and 6-B	
Soybean	Subgroup 6-C	
Tomato or bell pepper	Group 8	All are fruiting vegetables.
Cucumber	Subgroup 9-B	All are cucurbit vegetables; residues in melon and pumpkin expected to be lower because of removal of rind
Cantaloupe or Winter squash	Subgroup 9-A and pumpkin	
Orange	Group 10	Fruit will be peeled before analysis by PDP.
Apple or Pear	Group 11	All are pome fruits.
Peach	Group 12, except cherries (sweet and tart)	All are stone fruits.
Grape	Kiwifruit	Based on similar cultural practices.
Wheat	Group 15, except corn, rice, or wild rice	All are small grain crops or closely related thereto,
Milk	Meat	Metabolism study must indicate that residues in meat, fat, and meat-by-products will likely be equal to or lower than residues in milk. If dermal use is allowed on beef cattle, then it must be permitted and used on dairy cattle as well.

PDP has not analyzed eggs or fish, but surveillance monitoring data from FDA include extensive analysis of eggs and fish and indicate that NMC residues would not be expected to occur in significant amounts on these two foods. Consequently, residues in the revised NMC CRA were assumed to be zero. These foods account for about 2% of the per capita consumption of children 1-2 years old.



PDP has analyzed high fructose corn syrup and found no NMC residues but has not analyzed any other sugar or syrup sources. The FDA TDS has analyzed refined sugar and maple sugar and found no NMC residues in 46 market baskets surveys (FDA, 2007b). Knowledge of the highly refined nature of sugars and syrups supported by the limited residue data mentioned above is the basis for assuming that negligible residues of NMC pesticides occur in sugars and syrups. Therefore, residues were assumed to be zero for those foods derived from sugarcane, sugar beet, and maple. These foods, in total, account for about 2% of the per capita consumption by children 1-2 years old.

In summary, food forms, not included in the current assessment, account for only slightly more than 2% of the per capita consumption by children 1-2 years of age and the revised NMC CRA accounts for and incorporates almost 98% of the per capita food consumption by 1-2 year old children. No one single food form excluded from the assessment accounts for a significant portion of the consumption. Most of the foods that are not included in the assessment are considered very minor consumption items and include such commodities as mango, sunflower seed, peppermint, and pomegranate.

5. Method of Estimation of Cumulative Food Risk

The cumulative dietary exposure was estimated using the Dietary Exposure Evaluation Model-Food Commodity Index Database (DEEM-FCID™) software (Exponent, 2007). Estimation of dietary exposure was accomplished by combining distributions of pesticide concentrations on foods from USDA PDP with distributions of food consumption from USDA CSFII. The primary advantage of using distributions of pesticide concentrations and consumption values to assess cumulative exposure is that distributions of exposure values are obtained that represent a distribution of realistic scenarios of exposure that describe both probabilities and magnitudes of multi-chemical cumulative exposure through the food pathway.

a. Overview of Single-Chemical Dietary Risk Assessment Process

The dietary exposure models currently used by the Agency for single-chemical assessments rely upon the food consumption data provided by CSFII consumption survey respondents. For any particular respondent's reported consumption, a Monte-Carlo simulation is performed in which a series of randomly-drawn residue concentrations is selected for each food commodity. The exposure from each food commodity is calculated by multiplying each randomly-selected residue value by the amount consumed, and the total daily exposure is



calculated by summing exposures within each individual across all commodities reported consumed by that individual, as depicted below in Equation (1).

$$\text{Dietary Exposure}_{(\text{mgai/kg bwt})} = \sum_{i=1}^n \text{Consumption}_{(\text{gm food/kg bwt})} \times \text{Unit Conversion}_{(1 \text{ kg food}/1000 \text{ gm food})} \times \text{Residue}_i_{(\text{mgai/kg food})} \quad (1)$$

where n = number of unique foods (or food commodities) consumed

This repeated sampling of pesticide residues is performed 5,000 times for each individual's reported food consumption and produces a distribution of 5,000 potential exposure estimates for each individual respondent. The exposure software keeps track of the total daily exposures for each simulated person-day and applies the corresponding survey weights to project the simulated person-days to a per capita level. It is from this distribution of total daily exposures that the exposure at any given percentile (e.g., 95th, 99th, or 99.9th) can be estimated.

b. NMC Food Residue Database

Equation (1) above is, in principle, fairly basic: it is the task of performing and keeping account of these necessary calculations -- particularly for a multi-chemical, multi-pathway cumulative assessment -- that can be cumbersome, complex, and tedious. The residue data used in this assessment consist of nearly 790,000 records of analytical data and sample information. The processing factors account for several thousand additional records of information. Calculations and algorithms are complicated by the fact that they must be done in such a manner that the risk assessor can "work backward" from the cumulative assessment results to identify contributors -- and their relative contributions -- to the overall cumulative risk, and such contributors must be able to be identified on a crop, pesticide, or crop-pesticide combination basis. Because of these issues, all the data manipulations performed as part of this cumulative assessment were conducted outside of the DEEM-FCID™ exposure software using relational database techniques in MS Access. The database used to conduct these cumulative residue calculations consists of, among other things, four major data tables^{7,8} as follows:

⁷ By maintaining all of the calculation inputs in separate tables in the database, it is possible to modify inputs or perform sensitivity analyses by simply replacing or adding data to the appropriate table. For example, a specific chemical can be omitted from the entire process by assigning it a value of zero in the RPF table. Specific chemical-commodity combinations can be selectively omitted by entering a zero value for that pair in the processing factor table. Specific food commodities can be eliminated from the assessment by removing the entries from the translation table.



- 1) Residue Data: contains essentially all of PDP sample and analyses data for NMC pesticides for the years 1994-2006. The table in Appendix II.C.2 contains summary information of PDP residue data on the NMC pesticides.
- 2) Processing Factors: contains all relevant processing factors for specific food form/chemical combinations. The table in Appendix [REF_Ref178097444 \r \h * MERGEFORMAT] is extracted from these data.
- 3) Relative Potency Factors: contains the relative potency factors for all chemicals of interest. This table also contains the chemical-specific FQPA safety factor and inter-species uncertainty factor, which are also used to adjust the relative potencies of the NMC residues.
- 4) Bridging (Translations): provides bridging links or translations between PDP commodity codes, such as AP (for "APple") and all corresponding DEEM-FCID™ food forms, such as *Apple, fruit with peel; Uncooked; Fresh or N/S; Cook Meth N/S*. This table also translates surrogate PDP commodities for other food forms, e.g., orange residue data are assigned to lemon food forms as described in the table found in Appendix II.C.4.

These four tables are linked through common fields, including pesticide codes and commodity codes. Calculation queries are coded into the MS Access database so that all the pertinent PDP samples records can be extracted, each calculation outlined above can be performed, and the results can be sorted and output in various formats for further analysis. A cumulative residue calculation query performs the cumulative calculations (described in the next section), extracting the various parameters needed from the four tables described above. The calculation is performed on all of the food samples that are of interest and the results are compiled in text files containing the cumulative distributions for each food commodity of interest. Each text file contains a header with sample information (number of values, number of detects, number of zeros, average of residues) and all cumulative residue values for a single food form, sorted in descending order. This permits the complete history of each cumulative residue value in the exposure assessment to be traced back to its origins. In this way, all of the sample collection and analytical information associated with a given PDP sample and all arithmetic adjustments used to produce a cumulative residue

⁸ The NMC food residue database is based on the same design as the one used for the OP CRA (USEPA, 2006a).



estimate can be traced to permit sensitivity analyses or food commodity contribution analyses to be performed.

c. Manipulation of Residue Data for Exposure Assessment

Equation (1) above describes the fundamental algorithm used to estimate exposure from dietary sources. In the case of a cumulative assessment in which it is important to account for *multiple* pesticides within a food commodity, the formula is modified to account for these multiple chemicals. As seen in Equation (2) below, the residues are expressed in (i.e., converted to) index-chemical equivalents and Equation (1) re-cast as follows:

$$\text{Dietary Exposure}_{\text{IE}} = \sum_{i=1}^n \text{Consumption}_i \times \text{Unit Conversion} \times \text{Residue}_{\text{IE}i} \quad (2)$$

(mgai/kg bwt)
(gm food/kg bwt)
(1 kg food/1000 gm food)
(mgai/kg food)

where n = number of unique foods (or food commodities) consumed

Two changes in terms are evident in this equation which reflects a multi-chemical (cumulative) approach: the term “Residue” is replaced with “Residue_{IE},” (for index-equivalent residue, or residue expressed in terms of the index chemical oxamyl) and the term “Dietary Exposure” is replaced with the term “Dietary Exposure_{IE}” (for index equivalent dietary exposure). More specifically: residues (and the resulting estimated dietary exposures) are represented in this new equation in terms of the **index chemical** (for the NMCs: oxamyl). This re-expression of residues in terms of index chemical equivalents is a fundamental principle of cumulative risk assessment and is used throughout this and all of OPP’s cumulative assessments. Such re-expression of residues in terms of the common index chemical is performed through the use of the **Relative Potency Factor (RPF)**⁹ described (and derived) in Chapter B of this document. More specifically: the concentration of each pesticide in a given PDP food commodity sample is adjusted by multiplying that concentration by a RPF to obtain the equivalent residue expressed in terms of the index chemical. This new calculated residue is the **Index Equivalent Residue (Residue_{IE})** appearing in the above equation and the dietary exposure estimate resulting from combining Residue_{IE} and consumption is the **Index Equivalent Exposure (Dietary Exposure_{IE})**

The following two-step procedure provides additional detail with respect to how this calculation is performed for an individual PDP

⁹ The RPFs are also adjusted to account for the additional sensitivity of children compared to adults and humans compared to rats based on the chemical-specific FQPA and inter-species uncertainty factors, respectively. If additional toxicity data to quantify these safety factors are not available or lacking, a default value of 10 is assigned to each of these safety factors. Refer to Section B for details regarding the calculation of chemical-specific RPFs, FQPA safety factors, and inter-species uncertainty factors



sample. This process is repeated for each and every PDP sample included in the food assessment.

Step 1: For each pesticide in the cumulative assessment group, an Index Equivalent Residue (Residue_{IE}) is calculated for every residue in a particular PDP sample by multiplying the residue value by the chemical-specific processing factor (PF_i) for the food form of interest and the chemical-specific Relative Potency Factor (RPF_i):

$$\text{Residue}_{IEi} = \text{Residue} \times \text{PF}_i \times \text{RPF}_i \quad (3)$$

where i indicates an individual pesticide in the cumulative assessment group

Step 2: The cumulative Residue_{IE} for an individual PDP sample is then calculated by summing the individual Residue_{IEi} of all the pesticides in the cumulative assessment group found in that sample:

$$\text{Cumulative Residue}_{IE} = \sum_{i=1}^n \text{Residue}_{IEi} \quad (4)$$

where n = the number pesticides in the cumulative assessment group

The above-described procedure is critical in maintaining sample-by-sample integrity. By summing residues expressed in index-chemical equivalent concentrations on a sample-by-sample basis, capturing the co-occurrence of residues on the same sample is assured, and the ability to appropriately account for certain pesticides to be used (or not be used) on the same commodity is concomitantly enhanced.

These distributions of cumulative residues (expressed in terms of index chemical equivalents) are treated as distributions of representative residues and linked to all appropriate food forms. Finally, as described previously, these cumulative residues -- now expressed in terms of index-chemical equivalents -- are combined with a distribution of daily food consumption values via a probabilistic, Monte Carlo simulation using the DEEM-FCID™ software. The probabilistic combination of food consumption distributions and food residue distributions produces distributions of estimated exposures for OPP's standard age groups (Infants < 1, children 1-2, children 3-5, children 6-12, youths 13-19, adults 20-49, adults 50+ years old, and females 13-49 years old). This process has been described in public documents and proceedings of the FIFRA Scientific Advisory Panel (FIFRA SAP, 2000a).

d. Assumptions



The input residue data were drawn from the PDP data base. The PDP program tests different commodities for various pesticides in 10 states throughout the U.S. The residue data from 1994 to 2006 were used in this assessment unless otherwise noted. The assumptions in this revised NMC CRA, which are summarized below, are essentially identical to those used in the preliminary NMC CRA.

1) Although PDP has conducted single-unit sampling for limited crops (e.g., individual apple and pear samples) since 1998, only the residue data from composite samples (e.g., 10 pounds of apples or pears) were utilized in this assessment. Since a single composite sample can contain several individual servings of some foods, it is implicitly assumed that all these single servings have residues no more or less than the composite residue (average value). For this revised NMC CRA, it is assumed that residues reported on composite homogenates adequately reflect the residues in any given single serving contained in that homogenate. Therefore, no attempt was made to "decomposite" residue values to simulate residues that might be present in the single servings contained in the PDP composite sample.

2) PDP generally uses multi-residue methods to simultaneously analyze food commodity samples for several pesticides in single sample¹⁰. However, occasionally, for various reasons, not every sample is analyzed for every single pesticide. In instances where a pesticide is not analyzed in a sample, the pesticide is assumed to have a residue of zero. Although not every single pesticide is analyzed on every sample, PDP attempts to analyze for pesticides that are registered on the food commodity of interest. For each pesticide, generally only a small percentage (less than 10%) of the samples of a single commodity is not analyzed for all residues.

3) All residue analyses are subject to the limitations of the sensitivity of the analytical methods. Many of the samples analyzed are reported as being below the limit of reliable detection of the analytical method. It is usual practice in Agency single chemical assessments to assume that residues in non-detectable samples are present at one-half the limit of detection (LOD) of the analytical method in samples that were potentially harvested from treated fields. Thus, for purposes of estimating residues in samples reported as less than the LOD, a proportion of the samples equal to the estimated percent crop treated is assigned a residue level of one-half LOD and the remaining samples, which are assumed to come from untreated crops, are assigned a residue value of zero. This procedure becomes problematic for a cumulative assessment. It is not enough to simply estimate the percent

¹⁰ The table in Appendix II.C.7 contains summary information with respect to the co-occurrence of NMC pesticide residues in the PDP commodity samples.



crop treated for each of the pesticides in the cumulative assessment; it is also important to consider the potential for co-occurrence of residues of multiple residues on the same crop. In the case of the NMC pesticides, we assessed the impact of incorporating one-half LOD values for non-detects in the cumulative assessment. The food portion of the NMC assessment was conducted using the two extreme default assumptions: all non-detects = 0, and all non-detects = $\frac{1}{2}$ LOD for the chemical most frequently detected in each PDP commodity. The most prevalent detected chemical was selected because it is reasonable to assume that chemical would also have the greatest number of residues below the LOD. The result of this comparison confirmed that the assumption of zero values for all non-detects did not significantly impact on the results at the higher end of the cumulative exposure distributions. For additional information regarding this sensitivity analyses, refer to the Risk Characterization chapter.

4) The sample-by-sample method of summing residues relies on the PDP sampling procedures to adequately capture the temporal and geographic variations in agricultural practices and pesticide use. This procedure recognizes that the PDP sampling protocols are designed in such a way as to reflect the foods available to the public for consumption in different regions of the country throughout the year.

5) This assessment uses PDP residue data collected over a 13 year period, (1994-2006) to maximize the number of food commodities in the assessment and to minimize the sensitivity of exposure estimates to year-to-year variations in pesticide usage (e.g., atypical pesticide residues in a commodity due to unusual pest pressures). However, including pesticide residues over an extended period of time introduces an issue related to temporal correspondence of pesticide residues in various food commodities. Since PDP cannot sample every commodity every year, OPP relies upon residues in food samples collected in different years. In some cases, the residues in one food may be only one or two years older than residues in another food. In other cases, the food residues may have been sampled several years apart. Temporal correspondence of pesticide residues may be important to consider since acute dietary assessment consider foods eaten over relatively short time period, such as 24 hours. For example, it is not readily obvious if it is appropriate to model 24-hour dietary exposure based on pineapples grown in 2002 and cranberries grown in 2006.

6) In chemical-specific dietary exposure assessments, OPP routinely translates residue data from one food commodity to related ones if the pesticide use patterns are similar on these commodities. For example, data on cantaloupe are often used as surrogate data for honeydew and other melons. For a cumulative assessment, in which a



grower has a choice of several chemicals from the cumulative assessment group, these translations of data become more difficult. In the revised NMC CRA, translations of the residue data were made using the surrogation scheme in HED SOP 99.3 (USEPA, 1999b) to ensure representation of the maximum number of commodities possible. The cross walk between crops is presented in the table in Appendix [REF _Ref178097614 \r \h * MERGEFORMAT].

6. Estimation of Acute Exposure Using DEEM-FCID™ Software

Residue distribution files were entered in the DEEM-FCID™ software for a Monte Carlo analysis. The Monte Carlo analysis was conducted by an iterative process of multiplication of residue concentrations on foods, expressed in index chemical equivalents, by one-day consumption of these foods, as reported by all individuals in CSFII. This process used all individuals reporting in the consumption survey for both days of the survey and the exposures were calculated as mg/kg body wt/day.

DEEM-FCID™ uses publicly available USDA/EPA recipes for conversion of foods (e.g., lasagna) reported on an “as eaten” basis in the survey to the recipes’ component commodities (e.g., tomatoes, wheat, beef, milk, etc.) for which residue data are available. The use of DEEM-FCID™ for dietary exposure analysis has been described previously in public, technical briefings on pesticide risk assessments for pesticides in the re-registration process as well as to the FIFRA Scientific Advisory Panel (SAP). The detailed functioning of DEEM-FCID™ has also been described in previous SAP presentations (FIFRA SAP, 2000a).

7. Results

[REF _Ref177963189 \h] summarizes the DEEM-FCID™-generated estimated dietary (food only) exposures from the revised NMC CRA.

Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Summary of Probabilistic Analysis of Distribution of the Cumulative Dietary Exposures and Risk from Use of *N*-Methyl Carbamate Chemicals on Food Crops^a

Population	95 th Percentile		99 th Percentile		99.9 th Percentile		Percentile at which MOE=10
	Exposure (mg/kg)	MOE	Exposure (mg/kg)	MOE	Exposure (mg/kg)	MOE	
U.S. Population	0.0004	404	0.0023	79	0.0115	15	>99.9
All infants < 1 yrs	0.0005	342	0.0024	74	0.0106	16	>99.9
Children 1-2 yrs	0.0013	141	0.0051	35	0.0229	7.9	99.848
Children 3-5 yrs	0.0010	185	0.0044	40	0.0209	8.6	99.870
Children 6-12 yrs	0.0006	323	0.0028	63	0.0145	12	>99.9



Youth 13-19 yrs	0.0003	576	0.0017	106	0.0098	18	>99.9
Adults 20-49 yrs	0.0001	1278	0.0008	236	0.0042	42	>99.9
Adults 50+ yrs	0.0002	1035	0.0009	193	0.0044	40	>99.9
Females 13-49 yrs	0.0004	505	0.0019	97	0.0101	17	>99.9

^aExposure is in mg/kg/day of oxamyl equivalent residues.

Exposures and MOEs (Margins of Exposures) are presented for the U.S. General population and the following sub-populations: infants < 1 years, children 1-2 years, children 3-5 years, children 6-12 years, youth 13-19 years, adults 20-49 years, adults 50+ years and females 13-49 years. In addition, the percentile at which the MOE equals 10 is provided. The summary results are provided for three percentiles in the estimated distribution of exposures: the 95th percentile, 99th percentile, and 99.9th percentiles of exposure. The exposure values are expressed in terms of index-chemical equivalents. MOEs range from 7.9 (children 1-2 years) to 42 (adults 20-49 years) at the 99.9th percentile of exposure. For children 1-2 years, an MOE of 10 is reached at the 99.848th percentile; for children 3-5 years, this MOE is reached at the 99.870th percentile.

[REF _Ref177963249 \h], [REF _Ref178097653 \h * MERGEFORMAT] (for children 1-2 years old) and Figure 1.C-2 (for children 3-5 years old) provide additional information with respect to the contributors (in terms of crops, pesticides, and crop/pesticide pairs) to exposure. Appendix II.C.6 provides additional detailed information regarding the relative contribution of all crop/pesticide pairs for children 1-2 years old, the highest exposed sub-population.

Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Relative Exposure Contribution from Foods for Children 1 to 2 Years Old (At 99.8th Percentile of Exposure and Above)

Food	Percent
Potato	28.4%
Peach	14.4%
Strawberry	11.1%
Spinach	10.4%
Watermelon	6.7%
Pear	5.3%
Cucumber	3.4%
Cantaloupe	3.2%
Grape	3.0%
Bean, snap	2.4%
Nectarine	2.2%
Orange	1.7%
Apple	1.6%
Lettuce, head	1.3%
Total	94.8%^a

^aNo single remaining commodity contributes more than 1% to the total exposure.

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Figure I.[STYLEREf 2 \s]-[SEQ Figure * ARABIC \s 2]. Relative Contribution of Crop/Chemical Pairs to Top 0.2 Percentile of Cumulative Distribution for Children 1-2

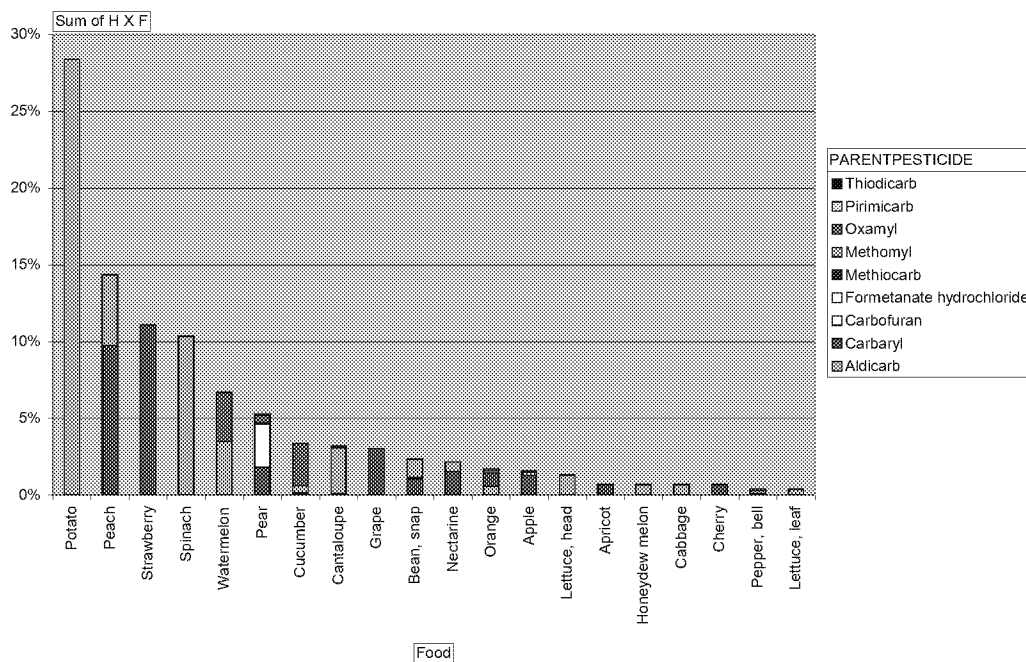
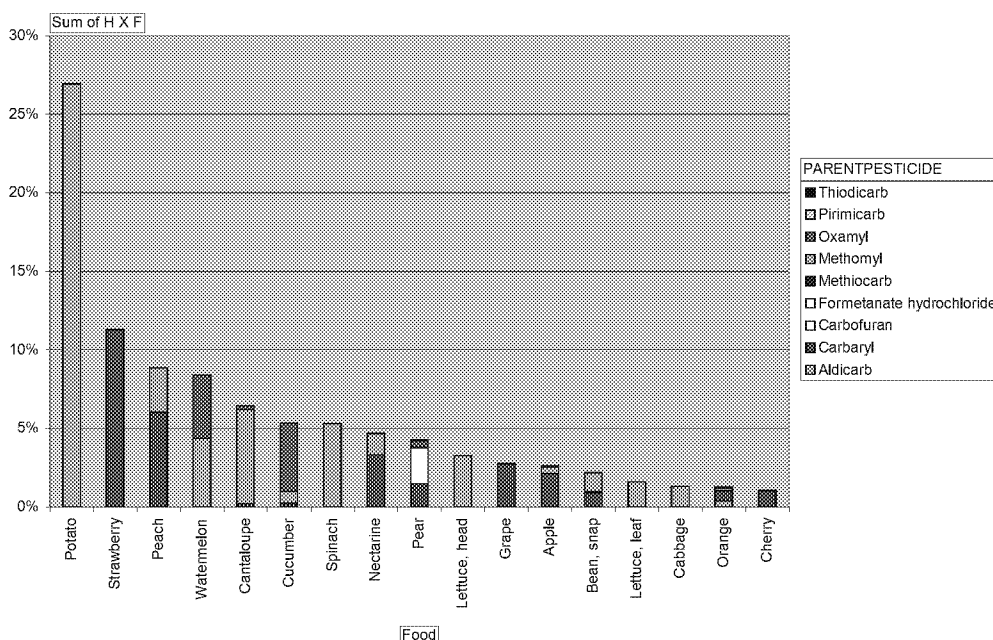


Figure I.[STYLEREf 2 \s]-[SEQ Figure * ARABIC \s 2]. Relative Contribution of Crop/Chemical Pairs to Top 0.2 Percentile of Cumulative Distribution for Children 3-5



In evaluating exposure through food, OPP concludes that a few uses of NMC pesticides on food crops generally play a larger role in the results of the assessment. These include aldicarb on potato; carbaryl on peach and strawberry; and methomyl on cantaloupe, watermelon, peach, spinach, and strawberry. However, evaluation of the total risk from exposure to NMCs in foods indicates that the cumulative MOEs from exposure to NMCs do not raise a concern.

In addition to exposure estimates generated by DEEM-FCID™ software, the Agency has conducted a similar assessment using LifeLine software which is also publicly available. Similar exposure estimates to those generated by DEEM-FCID™ were obtained with this software. It is important to recognize that exposure estimates between DEEM-FCID™ and LifeLine are not expected to be identical since there are important design differences relating to different reference populations, binning methodologies by which each model groups individuals, reference population bodyweights, and model (or sampling) weights. Nevertheless, exposure estimates agree to within several percent. The operation of this software and the exposure estimates produced by LifeLine are described in Appendix [REF _Ref178097749 \r \h].

Finally, it is important to note that the exposure estimates and associated MOEs presented in Table I.C-3 represent the Agency's "baseline" assessment described in this on exposure through the food pathway. There are a number of assumptions that are reflected in this baseline assessment that might affect exposure and MOE estimates that



are important to consider in evaluating risks associated with this pathway. Specifically:

- ❑ The baseline assessment presented here represents virtually all available PDP data (1994-2006)¹¹ and thus represents an average exposure over this time period. The Agency has performed an equivalent assessment using just the most recent years of PDP (2002-2006), the result of which are discussed in Chapter G. To the extent that more recent PDP pesticide residues more accurately reflect current (and future) conditions, exposure estimates conducted with only this more recent data might be more reflective of the current (and future) risk situation.
- ❑ The baseline assessment presented here assumes that PDP samples with non-detectable residues do not contain residues (i.e., residues are zero). In reality, residues may be present and – to the extent they are – exposures presented in Table I.C-3 may be underestimates of actual exposure.
- ❑ For the baseline assessment, carbofuran was assumed to be present only on commodities with import tolerances (banana, rice, coffee, and sugarcane) since the Agency has determined that all domestic uses are ineligible for reregistration (USEPA, 2006e). Pesticide residue concentrations on uses that are being cancelled were assumed to be zero to represent future carbofuran use.
- ❑ The DEEM-FCID™ model does not separate eating events by time and instead sums all eating (and thus exposure) events that occur over a 24-hour time frame. For this Revised NMC CRA, no account is made for the potential reversal of acetylcholinesterase inhibition that would be expected to occur if two or more exposure events are separated in time to such a degree that substantial recovery of AChE inhibition occurs. Such an assumption would be expected to over-estimate risk to the extent that some recovery of AChE activity would occur between exposure occasions.

To account for and evaluate the effect of the above-listed factors on the baseline exposure and risk estimates, the Agency has performed additional analyses which represent “extensions” (sensitivity analyses)

¹¹ Although additional PDP data are available for 1992 and 1993, these data represent the first years of the program which are limited in scope, completeness, and representativeness.



to this baseline assessment and permit the Agency to better evaluate how these assumptions and policy choices might affect its exposure and risk estimates. These activities and their results are more fully described in the Risk Characterization chapter of this document.

8. Summary

The cumulative dietary exposure due to the use of NMC pesticides on food crops was assessed using residue monitoring data collected by PDP. Oxamyl was selected as the index chemical and the residue values for the other NMC chemicals were converted to index chemical equivalents using the Relative Potency Factor method. Residue data were collected on approximately 80 food commodities monitored by PDP between the years of 1994 and 2006. Food processing factors were applied to specific chemical-commodity pairs to extend these data for use on more food forms (e.g. boiled, baked, fried, etc.). When appropriate, the PDP residue data were further extended to similar commodities which were not sampled in PDP. Food consumption data were obtained from the USDA Continuing Survey of Food Intakes by Individuals (CSFII), 1994-96/1998.

The residue data were compiled as distributions of cumulative residues of index chemical equivalents that were, after adjustment for processing, summed on a sample-by-sample basis. These residue distributions were combined with a distribution of daily food consumption values via a probabilistic procedure to produce a distribution of potential exposures for the general U.S. population and various sub-populations. The estimated exposures (expressed in oxamyl-equivalents) are shown in [REF _Ref177963189 \h]. An analysis of the relative exposure contribution from foods for children 1 to 2 years at or above the 99.8th percentile of exposure is presented in [REF _Ref177963249 \h * MERGEFORMAT].

The results of the baseline assessment indicate that all subpopulations, except children 1-2 and 3-5 years of age, exceed an MOE of 10 at 99.9th percentile of exposure. However, an MOE of 10 was reached for children 1-2 and 3-5 at the 99.848th and 99.870th percentiles of exposure, respectively. EPA concludes that the cumulative MOEs from exposure to NMCs in foods do not raise a concern. (Refer to Chapter G on Risk Characterization for a complete discussion of the rationale for this conclusion.)



D. Residential NMC Cumulative Risk

1. Introduction

The Office of Pesticide Programs (OPP) employed a calendar-based model (Calendex™) to address the temporal aspects of the residential use of pesticides. A calendar-based approach provides the ability to estimate daily exposures from multiple sources over time to an individual and is in keeping with two key tenets of aggregate risk assessment: 1) that exposures -- when aggregated -- be internally consistent and realistic; and 2) that appropriate temporal and geographic linkages or correlations/associations between exposure scenarios be maintained. The Calendex™ software allows OPP to delineate the critical timing aspects of seasonal uses of NMC insecticides that result in exposure to pesticides during the year. Calendex also enables OPP to identify potential risks caused by co-occurrence of exposures from multiple routes and pathways (e.g., near simultaneous same-day exposures through drinking water and residential uses). This includes the exposure from home lawn and garden treatments and pesticides used on golf courses.

In the revised NMC CRA, the temporal aspects of residential pesticide applications were evaluated by relying on information from a variety of sources including registered labels, survey data, and publicly available information provided by State Cooperative Extension Services. These information resources were comprehensively used to identify information such as frequency of applications and the seasonal appearance of target pests. OPP also relied on a national pesticide usage diary survey delineating day of application of registered pesticide products. This longitudinal survey also captures incidence of co-occurrence of residential uses of the same pesticide or similar pesticides on the same day. The survey was conducted by the National Family Organization on behalf of the Residential Exposure Joint Venture (REJV). Additional details regarding all use information used in the revised NMC CRA is presented in Appendix II.D.1.

In addition to the use practice and timing information described above, information regarding residues, exposure and standard exposure factors (such as breathing rates and activity duration) are required. In nearly all cases, the residential exposure scenarios in this assessment were developed using proprietary residue and exposure data. Exposure factors such as breathing rates and durations of time spent outdoors were taken from various sources including Agency's Exposure Factors Handbook (USEPA, 1997a). For the majority of residential uses



considered in this assessment, the full range of exposure values – expressed as uniform, log-normal, empirical, or cumulative distributions – are used, where appropriate, rather than relying on point estimates. While the dietary and drinking water assessments address only the oral exposure route, the residential assessment considers the dermal and inhalation exposure routes as well as the oral route, which is based on the mouthing behavior of young children.

2. Scope of Regional Assessments

Three NMC pesticides in this cumulative assessment have residential uses: carbaryl, methiocarb, and propoxur. More specifically, the residential uses included in this assessment are:

- carbaryl on turfgrass (residential lawns and golf courses);
- carbaryl on fruit trees, vegetable and flower gardens, and ornamental trees and shrubs;
- carbaryl impregnated pet collars;
- propoxur impregnated pet collars;
- methiocarb use in ornamental gardens as a snail and slug bait.

All other *N*-methyl carbamate residential uses are considered minor contributors to exposure and therefore were not included in this assessment.¹² Additionally, the Agency recently received voluntary cancellation of all propoxur indoor spray uses that may result in non-occupational exposure for children (USEPA, 2007c). Therefore, the

¹² For example, propoxur is registered for several residential uses including; outdoor use as a crack and crevice and spot spray, and indoor uses as a containerized bait, paste, shelf paper, or strip. For the outdoor crack and crevice and spot spray uses, applications are typically made along window sills or in pavement cracks; to ant hills and wasp nests. Additionally, the labels for the shelf paper, paste, and strip products restrict use to inaccessible areas. For instance, the paste products are packaged in a pre-filled disposable syringe. Applications are made by pushing the syringe plunger into cracks and crevices in counters, tables, shelving, drawers, under sinks, and around pipes, stoves, and electrical boxes. The propoxur shelf paper products are used in sewers, cabinets, or storage areas around garbage, under sinks, in basements, or other secluded areas where insects congregate. The containerized bait, paste, strip, and shelf paper products, in addition to the outdoor spot uses, are expected to result in very low exposure and therefore are not included in this assessment. Specifically, since the shelf paper, paste and strips are used only to inaccessible areas; children's dermal or hand-to-mouth exposure is not expected. Because the bait is packaged in a child-proof container, use in and around the home also is expected to result in negligible exposure. Additionally, the use of carbaryl for oyster beds in Washington State was assessed in the carbaryl RED. Since the oyster bed use is restricted to one area of the country, and since the assessment of this use indicated low exposure and risk, this use is considered to be a minor contributor to overall risk and therefore is not included in the revised NMC CRA.



propoxur indoor crack and crevice scenario, included in the preliminary NMC CRA, has been removed from this assessment.

In this revised NMC CRA assessment, only the Southeast region of the United States is considered (see [REF _Ref177958786 \h * MERGEFORMAT] below). While insect growth may slow during the winter months in the South, unlike other regions of the country, there is no period of dormancy. Since the growing season is longer in the South and the associated pest pressures are therefore greater, this assessment provides a worst case estimate of exposure.

Figure 1. [STYLEREf 2 \s]-[SEQ Figure * ARABIC \s 2]. Pesticide Cumulative Assessment Regions



3. Residential Scenarios

The Residential Scenarios addressed in this document represent critical NMC uses that have the potential for significant exposure when considered in a cumulative assessment. A brief description of each of the use scenarios covered in this assessment is provided below.



a. **Lawn Care**

Carbaryl (adult applicator and adult and child post-application exposures)

Carbaryl may be applied by homeowners or professional lawn care operators (LCO). Granular, dust, and sprayable applications can be made by consumers using push-type spreaders, ready-to-use (RTU) shaker cans, and hose-end sprayers respectively. OPP has recently amended the use pattern of carbaryl (see Table II.A). The label changes restrict broadcast lawn application to granular formulations. However, spot treatments with the liquid formulations are permitted. Liquid products will be packaged in ready-to-dispense containers that treat areas of no more than 1000 square feet. The current assessment incorporates the recent label changes for the use of carbaryl on residential lawns.

Dermal and inhalation exposure was assessed for homeowners loading, and applying carbaryl to residential lawns. This assessment also considered dermal post-application exposure for adults and children contacting treated lawns. Additionally, oral non-dietary exposure (hand-to-mouth) was considered for toddlers transferring treated-turf residues from their hands to their mouths. Post-application exposure was assessed for the granular broadcast use of carbaryl but not for the liquid spot treatment uses.

b. **Vegetable Gardens**

Carbaryl (adult applicator and adult and teenagers post-application exposures)

Dust, liquid, and granular formulations of carbaryl may be applied to garden vegetables using RTU shaker cans, handwands, trigger pump sprayers or hose-end sprayers. (Note that recent label changes require all home garden products formulated as either a dust or a granular to be packaged in ready-to-dispense containers (see Table II.A). Dermal and inhalation exposure was assessed for homeowners mixing, loading, and applying carbaryl to vegetable garden plants based on data for the liquid and dust formulations. The use of liquid and dust data for granular applications is conservative and results in higher estimated exposure. Post-application dermal exposure also was considered for adults and teenagers re-entering treated gardens to harvest vegetables or perform maintenance tasks (such as weeding).

c. **Ornamentals**

Carbaryl (adult applicator and adult and teenager post-application exposures)



Carbaryl may be applied as a dust to ornamental plants using a RTU shaker can. Note that recent label changes require all home garden products formulated as either a dust or a granular to be packaged in ready-to-dispense containers. Carbaryl may also be sprayed on ornamentals (flowers, trees and shrubs) using a small handwand or hose-end sprayer. The current assessment evaluated exposure for homeowners applying liquid formulations of carbaryl via the handwand sprayer since chemical-specific applicator data suggests that the handwand sprayer resulted in similar yet higher exposure than the hose-end sprayer. The data used to assess this scenario account for homeowners applying sprays below the waist as well as overhead. Dermal and inhalation exposure was assessed for homeowners mixing, loading, and applying carbaryl to ornamental garden plants. Post-application dermal exposure also was considered for adults and teenagers performing ornamental garden maintenance tasks (such as pruning).

Methiocarb (adult applicator exposure)

Methiocarb may be applied to soil areas in and around ornamentals for the control of snails and slugs. This product is formulated as bait applied as a broadcast application over plant foliage or to the soil surrounding ornamental plants. Exposure from this use is expected to be minimal. Therefore, post-application exposure was not evaluated for this scenario.

d. Fruit Trees

Carbaryl (adult applicator and adult and teenager post-application exposures)

Carbaryl may be sprayed on fruit trees using a handwand or hose-end sprayer. The current assessment considers dermal and inhalation exposure for handwand applications only. Chemical specific applicator data for this use indicate greater exposure resulting from handwand applications than from hose-end sprayers, and therefore is considered to be worst case. Post-application dermal exposure was assessed for adults and teenagers harvesting fruit and performing fruit tree maintenance tasks (such as pruning).

e. Pet Collars

Carbaryl (adult and child post-application exposures)

Propoxur (adult and child post-application exposures)

Carbaryl and propoxur are formulated as impregnated pet collars. Post-application dermal exposure was considered for adults and children contacting (hugging, petting) treated pets. Oral non-dietary exposure



also was assessed for toddlers contacting treated pets and transferring residues from their hands to their mouths.

f. **Golf Course**

Carbaryl (adult and teenager post-application exposures)

Carbaryl is also used on golf course turf. Golf course workers may apply liquid or granular formulations of carbaryl as a broadcast application to fairways, greens and tees. Post-application exposure was assessed for adults and teenagers playing rounds of golf on courses treated with the sprayable formulations of carbaryl.

4. **Exposure Routes/Scenarios Considered**

The routes of exposure considered in this cumulative assessment varied depending on certain application and post-application exposure activities that were determined to be age group-specific. Since cumulative risk assessments do not include occupational risks, applicator exposure is not assessed for the golf course scenario. However, EPA does perform separate occupational risk assessments for such exposure scenarios. The specific exposure routes and pathways/scenarios are summarized and described in additional detail below in Table I.D-1:



Table I.[STYLEREf 2 \s]-[SEQ Table * ARABIC \s 2]. Specific Exposure Routes and Pathways/Scenarios

Scenario	Population	Applicator			Post Application		
		Oral	Dermal	Inhalation	Oral	Dermal	Inhalation
Lawn/Turf	Adults		X	X		X	
	Children 1-2				X	X	
	Children 3-5				X	X	
Home Garden	Adults		X	X		X	
	Youth 13-17					X	
	Children 1-2						
	Children 3-5						
Indoor (c&c)	Adults		X	X		X	X
	Children 1-2				X	X	X
	Children 3-5				X	X	X
Pet Collars	Adults					X	
	Children 1-2				X	X	
	Children 3-5				X	X	
Ornamental Plants and Trees	Adults		X	X		X	
	Youth 13- 17					X	
	Children 1-2						
	Children 3-5						
Fruit Trees	Adults		X	X		X	
	Youth 13-17					X	
	Children 1-2						
	Children 3-5						
Golf Course	Adults					X	
	Youth 13-17					X	



a. Oral Route of Exposure

Toddler ingestion via hand-to-mouth activity was the only oral route of exposure considered in the residential portion of this assessment. Specifically, oral hand-to-mouth ingestion was considered only for children 1-2 and 3-5 years old for the lawn care and pet collar scenarios. OPP acknowledges that there are very limited data on exposure to young children; in general, however, children ages six and older no longer exhibit mouthing behavior to the degree seen in younger children (Freeman et al, 2001). In addition, OPP recognizes that non-dietary exposure may occur not only from hand-to-mouth activities but also from activities such as ingestion of soil and mouthing of grass. However, the latter two pathways were not considered in this assessment because these types of non-dietary exposures are expected to be small contributors to overall risk from residential NMC products¹³.

¹³ Typically, in single chemical human health risk assessment for pesticides, hand-to-mouth exposure is significantly higher than object-to-mouth (i.e., grass ingestion) exposure. However, in the carbaryl RED, the grass ingestion MOE for the lawn care scenario is 150 while the hand-to-mouth MOEs ranged from 71 to 720. Currently, the Agency does not have a methodology to assess grass ingestion exposure for granular lawn products. As a conservative assessment for granular turf products, the Agency used standard assumptions based on the use of surrogate liquid turf transferable (TTR) data. Specifically, the quantitative assessment of object-to-mouth exposure in the carbaryl assessment relies upon the assumption that residues on grass will be between 3 and 5% of the application rate (*HED Policy 12: Revised Residential SOP Assumptions, 2/2001*). This assumption is derived from liquid DFR turf studies for multiple chemicals using the dislodgeable foliar residue (DFR) method. The use of this method had been considered by investigators in the past, but is no longer used due to its high between-investigator variability. In addition the method had been used for measuring turf that is uniformly sprayed resulting in most grass leaves being contacted by the sprays. The DFR method involves shaking grass leaves in a dislodging solution for 20 minutes. The method itself is likely to be more an exhaustive estimate of transfer than may be expected when children's objects come in contact with turf treated with granular forms that are watered-in. Since all carbaryl liquid broadcast lawn products have been cancelled, the quantitative assessment for toddlers grass ingestion is highly conservative. Further, because the carbaryl hand-to-mouth MOEs for the lawn assessment were of concern when granular turf products were not watered-in, the Agency will modify all granular turf product labels to require watering-in after application. The target pests for the granular formulation are soil insects, consequently, it is important that the pesticide reach the soil for adequate control rather than remain on the grass. The Agency believes that watering-in, as demonstrated by the carbaryl handpress data, will significantly lower the residues of carbaryl on treated grass. However, the current methodology used to assess grass ingestion does not account for the reduction of residues following irrigation. For all of the above noted reasons, the Agency believes that grass ingestion exposure resulting from the use of carbaryl granular lawn products will result in minimal exposure and therefore was not included in the revised NMC CRA.



i. Modeling the Non-Dietary Ingestion Pathway

In the preliminary *N*-methyl carbamate cumulative risk assessment (preliminary NMC CRA), the non-dietary oral exposure pathway produced the lowest Margins of Exposure (MOEs), and would therefore be of greatest concern to the Agency. These low MOEs were mainly due to the incorporation of micro-activity data into our macro activity models (defined as human exposure models based on daily time step). The non-dietary ingestion pathway was the least refined of the residential exposure pathways modeled in the preliminary NMC CRA. This section highlights modifications made to the methodology used to assess this pathway. This refined methodology is based on comments and input from the FIFRA Scientific Advisory Panel, and the SHEDS and CARES developers.

The Calendex model used in the preliminary and the revised NMC CRAs is a macro activity model. Specifically, this model simulates exposures by randomly drawing age-appropriate values for each of the various exposure factors (e.g., exposure duration, frequency of hand to mouth events, surface area of hand mouthed per event, etc.) then multiplying these values together per the OPP Standard Operating Procedures (SOPs) for Residential Exposure Assessment algorithm (USEPA, 1997b). The distributions for many of these exposure factors were obtained from micro-activity data. For example, the distribution for frequency of hand-to-mouth events was based on data from observational studies in which all hand contacts were recorded as hand-to-mouth events, regardless of the fraction of hand mouthed. For the fraction of hand mouthed, no adjustment was made for the duration of time the hand remained in the mouth. As the August 2005 SAP panel discussed, utilizing such micro-activity data with macro activity models poses many challenges. For example, if two variables are negatively correlated (e.g., more frequent mouthing is associated with smaller areas of hand mouthed), then “modeling the product of two jointly distributed variables as independent draws will overestimate the variances...or overestimate exposure at the high end.” Similarly, “fixing the residue on a child’s hands (and/or other exposure factors) for a two hour play period...will yield ‘greater variability in the modeled distribution of exposures than a run that updates the residue concentration hourly during the exposure’”. (FIFRA SAP, 2005b).

As recommended by the SAP, the Agency is exploring the use of SHEDS-Multimedia for future probabilistic risk assessments. In the revised NMC CRA, Agency staff addressed shortcomings in the non-dietary oral pathway by modifying the probabilistic hand-to-mouth algorithm as discussed below. This modified algorithm is a product of a



collaborative effort between OPP scientists, and the developers of the SHEDS-Multimedia (Dr. Valerie Zartarian and Dr. Jianping Xue) and CARES models (Dr. Jeffrey Driver and Dr. Muhilan Pandian).

The refined algorithm for estimating daily hand-to-mouth ingestion in the revised NMC Calendex assessment is similar to the SHEDS-Multimedia and CARES Mass Balance algorithms in the manner in which it addresses residue replenishment between hand-to-mouth contacts. Specifically, the new algorithm establishes a maximum amount of residue which can be on the hand, or a maximum dermal hand loading. The amount of non-dietary oral ingestion increases with the exposure duration, the frequency of hand-to-mouth events per hour, and the surface area mouthed per event, while the hand loading serves as an upper constraint on oral ingestion between replenishment events.

New Hand-to-Mouth Algorithm

The following equation is the algorithm used in the Revised NMC CRA:

[EMBED Equation.3]

HR/2 = initial residues available on one hand [mg/day]
SA mouthed fraction = surface area of hand mouthed [unitless].
N_Replen = number of replenishment intervals per day. This is equivalent to the values used for Duration [hrs/day] in the preliminary NMC CRA since the residues are assumed to be "replenished" every hour of the exposure duration
SE = saliva extraction factor (i.e., mouthing removal efficiency) [unitless];
N_Events = number of hand-to-mouth contacts events per replenishment interval;

Each of these terms is discussed in detail below.

Hand Loading

Hand loading, or HR/2, is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA Child Specific Exposure Factors Handbook indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over (USEPA, 2002c, table 8-3). The algorithm assumes mouthing one hand at a time; therefore, hand loading residues are divided by 2.



Frequency of mouthing events and fraction of surface area mouthed

The distributions for frequency of mouthing events (N_{Events}) and the fraction of surface area of hand mouthed (SA mouthed fraction), are based on observational studies (see scenario-specific discussions in section I.D.6 for more details on the information sources used for these parameters). This algorithm allows for only one draw (per simulated day), therefore, the interpretation is that this behavior continues at the same rate for the entire exposure duration selected. In reality, a high-end mouthing frequency recorded over a short time interval (e.g., one hour) may not be likely to continue at the same intensity over a longer time period (e.g., 6 or 8 hours).

Saliva extraction factor (i.e., mouthing removal efficiency)

The saliva extraction factor (SE) indicates the fraction of residues that is removed during each mouthing event. The greater the removal efficiency (i.e., SE), the less residue remains on the hand after each mouthing event. For example, if the initial loading is 1000 ug on the thumb (part of hand mouthed), and the removal efficiency is 20%, then after one event, 200 ug is removed and 800 ug remains on the thumb; after two events, an additional 160 ug is removed ($=800 \times .2$), or a total of 360 ug ($=1000 \times (1 - (1 - .2)^2)$) is removed and ingested, and 640 ug ($=1000 \times ((1 - .2)^2)$) remains on the thumb.

The SE term is used in combination with the mouthing frequency term (N_{Events}) in the above equation as:

$$(1 - SE)^{N_{\text{Events}}}$$

This portion of the new hand-to-mouth algorithm expresses the percent of initial loading remaining on hand after N hand-to-mouth events or, equivalently, the percent of initial loading mouthed that is ingested after N hand-to-mouth events.

Replenishment Interval

In the preliminary NMC CRA, the non-dietary ingestion algorithm assumed complete replenishment between each hand-to-mouth event. This new algorithm is more comparable to the SHEDS-Multimedia and the CARES Mass Balance algorithms in addressing the replenishment. The new algorithm assumes that replenishment occurs only once every fixed time interval (SHEDS uses the Consolidated Human Activity Database (CHAD) time interval; CARES uses a daily time interval). Within each replenishment interval, a fraction of the remaining residues



are removed and ingested during each hand-to-mouth event. The total amount of residues removed and ingested increases with the SE, the number of events per interval, and with the number of replenishment intervals per day (or exposure duration).

In this new algorithm, the hand is fully replenished with residues from a contaminated surface (e.g., the lawn, pet or hard flooring), on an hourly basis. The replenishment frequency (hrs/day) and the mouthing frequency per replenishment interval (events/hr) are expressed in the same time unit (hr). Therefore, the same distribution, total exposure duration (hrs/day) was used in the preliminary NMC CRA. This algorithm may be generalized to model replenishment at different (fixed) time intervals.¹⁴

b. Dermal Route of Exposure

The dermal route was assessed for adults applying consumer pesticide products to lawns, gardens, fruit trees, and ornamental plants. For both children and adults, post-application dermal exposure was assessed for the lawn and pet collar scenarios. The dermal route was also assessed for adults and teenagers reentering treated vegetable and ornamental garden to perform maintenance (weeding, pruning) and harvesting activities. Similarly, exposure was assessed for adults and teenagers involved in fruit tree cultivation. Dermal post-application exposure also was assessed for adults and teens playing golf on treated courses.

c. Inhalation Route of Exposure

The inhalation route of exposure was considered for adult populations only. Specifically, inhalation exposure was assessed for adults applying pesticide formulations to lawns, vegetable gardens, ornamental plants and fruit trees.

¹⁴ For example, if it is assumed that the hand is fully replenished every half hour, then both variables (N_Replen and N_Events) would be constructed using 30 minutes as the unit for duration. Similarly, if one replenishment per day (N_Replen=1) is assumed, this new algorithm reduces to the CARES Mass Balance equation. This is demonstrated by replacing the number of replenishment intervals per day (N_Replen=1/day), and the total mouthing events per replenishment interval (events/day) with the equivalent terms (N_Events = FREQEvents/hr x Duration hrs/day) in the following equation:

$$Exposure = \frac{HR}{2} * SA_{mouthed_fraction} * 1 * [1 - (1 - SE)]^{Freq_{events/hr} * Duration_{hrs/day}}$$



5. Data Sources

Three basic types of data were considered in this assessment:

- pesticide use data;
- residue concentration and dissipation/decay data;
- exposure contact factor data.

These data are described in more detail below.

a. Pesticide Use Data

The probabilistic models require residential pesticide use inputs to aggregate exposure from multiple use scenarios. The percent of households applying the various products and the timing of those applications directly impact estimates of aggregate exposure. The REJV data can be used to generate empirically-based estimates to address those needs. Appendix II.D.1 provides further details regarding the REJV data. However, the REJV did not collect information on the purpose of use (pest treated), areas treated, or application rates. Since these factors may impact timing and frequency of application, REJV data was used in combination with professional judgment, product label information and pest pressure information from the Cooperative State Extension Services. The revised NMC CRA considered the Southeast Region of the United States for two reasons; 1) the growing season is longer in the South and the associated pest pressures are therefore greater, and 2) drinking water concentrations are highest in this region of the country. The residential and groundwater assessments are based on the most highly exposed localized areas within the southeastern region of the United States. Specifically, the drinking water exposure for Georgia was combined with residential exposure in Florida. Pest pressure data for Florida are assumed to address pest pressure for other areas of the country where NMC water concentrations are high (such as Georgia and North Carolina). Due to longer periods of pesticide use coupled with higher concentrations of NMC in ground water, this assessment provides a worst case estimate of exposure.

The revised NMC CRA focuses on post-application exposures for children, including the broadcast lawn and the pet collar scenarios. Examples of how pesticide use data were incorporated into these scenarios are discussed below.

i. Broadcast Lawn Scenarios



Current label revisions for carbaryl lawn care products restrict broadcast applications to granular formulations. Therefore, post-application exposure for children was assessed only for granular applications of carbaryl to lawns. The major turf pests treated with carbaryl are grubs, mole crickets, caterpillars, cinch bugs, scales, ticks, and a variety of spiders, and ants. However, pests that would mostly likely be treated with granular applications are mole crickets and white grubs. The other pests listed are more likely to be treated with spray applications. Therefore, this assessment focused on timing of applications for residential lawns treated for white grubs and mole crickets. Information from the University of Florida Cooperative State Extension Service indicates that grubs actively feed in Florida from April through October, depending on species and weather conditions. Additionally, tawny mole crickets become active in March, and granular applications are typically made in August and September. For these reasons, the broadcast lawn assessment considered the season of use to be early spring through fall. OPP assumed two applications to the lawn per year (based on REJV).

ii. Pet Collar Scenarios

Propoxur and carbaryl product labels indicate that pet collars are effective for 180 days and 120 days, respectively. Additionally, season of use is considered to be year-round since flea lifecycle information shows that in humid climates, fleas may be active year-round. Therefore, the pet collar assessment assumed that pet collars would be used year-round in southern climates.

b. Residue Concentration Data

Residue concentration data and associated pesticide decay/dissipation parameters were used to define the sources and magnitude of exposure resulting from human contact with transferable residues. In many cases, chemical-specific data were used to assess homeowner applicator and post-application exposure resulting from the registered uses of carbaryl. For the lawn and garden scenarios, data from the Outdoor Residential Pesticide Use and Usage Survey and National Gardening Association Survey (Johnson et al, 1999) submitted by the Outdoor Residential Exposure Task Force (ORETF) were also used. Surrogate data were used to determine exposure resulting from the ornamental garden use of methiocarb. Appendix II.D.2 contains a summary of all residue data used in the revised NMC CRA, as well as the derivation of various distributional parameters.



c. Exposure Factor (Contact) Data

Exposure factors such as the amount of time spent in an area, frequency of hand-to-mouth contacts, size of area treated, and location of residue source (lawn, garden, or indoor surface) are critical for estimating exposures to a given substance. Appendix II.D.2 contains a summary of exposure factors used in the revised NMC CRA, as well as the derivation of various distributional parameters. Unless otherwise noted, all distributions were truncated at the 99th percentile in order to avoid a distribution which contained values that were well beyond those deemed reasonable.

6. Exposure Scenarios

This assessment considered a variety of exposure scenarios for consumer applicator and post-application exposures. Each of these is described in additional detail below. Since it is difficult to determine typical rates for homeowner products, OPP used the maximum application rate, as allowed by currently registered labels, to assess exposure for all scenarios. (8 lbs ai/A was used for lawns and fruit trees; and 2 lbs ai/A was used for vegetable gardens and ornamentals.) [**REF _Ref178098685 \h**] summarizes the selected inputs for all scenarios.

a. Lawn Care Exposure Scenarios

i. Lawn Applicator Exposure

Only carbaryl has registered lawn care uses. Applicator exposure was assessed for homeowners mixing, loading, and applying a variety of carbaryl products to their lawns. There are two formulations of carbaryl that are available for lawn use: granular and liquid sprayable formulations. OPP has amended the use pattern of carbaryl and the current cumulative assessment incorporates these changes. The label changes restrict broadcast lawn application to granular formulations. However, spot treatments of the liquid formulation are permitted. All liquid products must be packaged in ready-to-dispense containers. Such formulations will limit spot treatments to areas of less than 1000 square feet.

Total exposure is calculated as the product of the unit exposure (UE) (either dermal or inhalation), the application rate, and the lawn size.

Unit Exposures: Both dermal and inhalation exposure routes were considered. ORETF studies were used for the granular broadcast and liquid spot treatment scenarios.



The ORETF submitted a report (Klonne, 1999) in which a variety of products were used on turf. In these studies, both homeowners and lawn care operators (LCOs) were monitored following broadcast applications to turf. All of the data submitted in this report were completed in a series of studies.

The two studies that monitored homeowner exposure resulting from granular spreader (Klonne, 1999/OMA003 Study) and hose-end sprayer (Klonne, 1999/OMA004 Study) applications were used in this assessment. Volunteers participating in these exposures studies were adult non-professionals who use pesticides on their own gardens and lawns. Many of the volunteers selected as subjects in these studies were members of garden clubs. All volunteers made their applications without specific instruction from the study investigators. Unit exposures estimated from these studies cover various clothing scenarios that range from wearing short pants and short-sleeved shirts, to long pants and long- sleeved shirts.

All dermal and inhalation unit exposure were normalized and expressed as milligrams exposure per pound of active ingredient handled (mg/lb ai) (referred to as unit exposures, or UE). The lognormal distributions of the UEs for the lawn applicator scenarios are shown in Table I.D-2.

Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Lognormal Distributions of Unit Exposures Used for Carbaryl Lawn Care Scenarios

Application Method	Exposure Route	Unit Exposure Distribution (mg/lb ai) LN(μ , σ)	Comments
Granular Rotary Spreader	Dermal	0.81, 0.57	This distribution was used for the broadcast lawn scenario
	Inhalation	0.0013, 0.0013	
Hose-end Sprayer on Turf	Dermal	8.4, 26	This distribution was used for the lawn SPOT treatment scenario ONLY
	Inhalation	0.022, 0.040	

NOTES:

LN(μ , σ) represents a lognormal distribution with μ = arithmetic mean and σ = arithmetic standard deviation. For lawn scenarios, information was derived from carbaryl-specific data and studies conducted by the ORETF. A more detailed explanation of the statistical analysis of this data is provided in Appendix II.D.2.

Application Rates: For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the lawn care scenario).



Area Treated: An important variable for estimating home-owner applicator exposure is the size of the lawn. OPP considered the average and median lawn sizes reported in a journal article by Vinlove and Torla (1995). The means and medians were ~13,000 ft². However, the authors noted problems interpreting the data since it is based primarily on low income houses and consists of adjustments of the lot size by the house's foundation (footprint) only. The data do not consider other structures such as decks or other green space such as gardens, which can reportedly reduce the lot size by up to 50%. Similar lawn sizes were noted in the ORETF survey (Johnson et al, 1999) with similar problems encountered with respect to confounding variables such as decks and other green spaces. For this assessment, OPP used a uniform distribution for lawn size bounded by 1000 ft² and 20,000 ft². The lower end of this range considers smaller lawns for residences such as town houses. The upper bound of 20,000 ft² (~ ½ acre) appears reasonable given the type of application equipment assumed to be used by residential applicators. Information from the ORETF survey also indicates that many pesticide users make spot treatments of insecticides. Similarly for spot treatments, OPP assumed a uniform distribution for treated area bounded by 100 ft² and 1000 ft².

ii. Lawn Post-Application Dermal Exposure

The fate of pesticides applied to turf, and subsequent human contact, is a key variable for assessing post-application dermal exposure and can be an important exposure pathway to consider as part of a cumulative assessment. This exposure pathway was evaluated here in the revised NMC CRA by using data from a number of available studies (described in more detail below). Briefly, post-application dermal exposure (mg pesticide) is calculated by multiplying the residue concentration on the lawn (mg/cm²) by the transfer coefficient (cm²/hour) derived from literature and other studies and the time spent on the lawn (hours/day). For this assessment, the transfer coefficient and the time spent on lawns were represented by a distribution of values while the residue concentration on the lawn was represented by a time series of concentration values (which accounted for residue degradation over time and incorporated the relevant half-lives or decay coefficients). Due to the label revisions, post-application exposure was considered for the granular broadcast treatments only.

Residue Data: There are chemical-specific turf transferable residue (TTR) data for granular formulations of carbaryl (Krolski, 2005). This study was designed to determine transferable residues of carbaryl from both irrigated and non-irrigated turf treated with SEVIN® 2G (see Appendix II.D.2 for study summary). Measured carbaryl residues rapidly declined over the first 4 hours and then leveled off or rose slightly after 12 hours. By the 24-hour sampling interval, the residues declined to



approximately 10 percent of the corresponding 0-time residue value and then steadily dropped to below 1.0 percent of the corresponding 0-time residue values by 3- to 5-days after treatment.

In order to provide a conservative estimate of exposure for the revised NMC CRA, only the samples in the above study from the non-irrigated site in Florida were used. This assessment assumes an initial concentration of 0.00021 mg/cm². Dissipation is based on a 0.8 day half-life, with residues set to zero 14 days after application. Although the carbaryl TTR studies show residues below 1% of the initial residues by 3- to 5-days after application, to provide a conservative estimate of exposure, it is assumed that carbaryl residues on the lawn would be available for up to 2 weeks after application.

Transfer Coefficients (TC): The transfer coefficients used in this assessment were developed by dividing the hourly dermal exposure (µg/hr) obtained from a set of activities by the measurement commonly referred to as turf transferable residues (TTR) (µg/ cm²). Since none of the dermal exposure studies used to estimate hourly exposure permitted direct calculation of the TTR, the transfer coefficients for this assessment were developed by assuming a transfer efficiency of at least 0.5% for granular formulations. This was done for two reasons:

- ☐ to make use of available dermal exposure measurements which are not influenced the methodology used to estimate TTR, and
- ☐ to make use of the available residue dissipation data for which there are no corresponding dermal exposure measurements

The 0.5% value is within the range of efficiency for the existing chemical specific TTR data described above. To account for the additional uncertainty of assuming a certain transfer efficiency to develop the transfer coefficients, TTR data having transfer efficiencies lower than 0.5% (for granular applications) were adjusted upwards to make up the difference in efficiency. If the transfer efficiency of the TTR data was higher than 0.5% for granular formulations, it was not adjusted.

For a more detailed discussion of the relationship of transfer coefficients and TTRs please refer to the "Overview of Issues Related to the Standard Operating Procedures for Residential Exposure Assessment" presented to the FIFRA Scientific Advisory Panel on September 21, 1999.



Transfer Coefficients used to assess children's exposure to treated turf:

One study was used to assess children's dermal exposure resulting from granular applications to residential turf (Vaccaro, 1996). In this study, a granular formulation of chlorpyrifos was applied, after which seven adults performed pre-choreographed activities intended to mimic a typical child's behavior.

The subjects performed these activities for a period of four hours beginning after the turf had dried. Turf had been treated earlier with a granular form of chlorpyrifos and exposure was estimated in the study by monitoring the amount of a chlorpyrifos metabolite – 3,4,5,6-TCP – excreted over the following period of 6 days. This method directly measures internal dose and was used to back-calculate a generic "to the skin" transfer coefficient by using chemical specific dermal absorption data for chlorpyrifos (Nolan et al., 1984). These data were further adjusted to account for differences in surface area of adults and children.

The study data discussed above was fit to a lognormal distribution with an arithmetic mean of 1970 cm^2/hr with a standard deviation of 1426 cm^2/hr . The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e. 7224 cm^2/hr for the granular application) in order to avoid a distribution which contained values that were well-beyond those that are deemed reasonable. (See Appendix II.D.2 for study summary and details of the distributional analysis.)

Transfer Coefficients used to assess adult exposure to treated turf:

The Vaccaro study data discussed above were also used to assess exposure to adults following granular applications.

The revised NMC CRA used a distribution of values for the transfer coefficient characterized by a lognormal distribution with an arithmetic mean of 5376 cm^2/hr and a standard deviation of 4717 cm^2/hr for the granular application. The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e., 23436 cm^2/hr) for the granular application. (See Appendix II.D.2 for study summary and details of the distributional analysis.)

Duration: Another important variable for addressing post-application exposure from home lawn treatment is the duration of time spent on lawns. In this revised NMC CRA, cumulative distributions of durations on lawns of up to two hours were used to address adult exposure on lawns. These data are presented in Table 15-64 of the



Exposure Factor's Handbook (EFH) (USEPA, 1997a); however, OPP notes that the percentiles above the 95th have the same values (121 minutes). A similar cumulative distribution was given for children ages one to five. In order to be protective of children and to address the uncertainty in the upper percentiles of the exposure factor data, OPP selected an empirical distribution (which was expressed as a cumulative distribution function) from EPA's EFH (Table 15-80) with a bound of 3.5 hours for children. This distribution represents the amount of time spent outdoors rather than just on lawns. This adjustment allows for additional time that children may spend outdoors (such as parks and schools) where there is potential for additional contact with treated turf.

iii. Lawn Non-Dietary Hand-to-Mouth Exposure

The assessment also incorporates exposure resulting from toddler hand-to-mouth activity on lawns. The revised NMC CRA incorporates a new algorithm to estimate hand-to-mouth exposure. Details of this algorithm can be found in Section I.D.4.i of this document.

Initial Hand Loading: Hand loading (HR/2) is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA Child Specific EFH (USEPA, 2002c) indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over. The algorithm assumes mouthing one hand at a time, therefore, hand loading residues are divided by 2.

Frequency of Mouthing Behavior: For the revised NMC CRA, the frequency of hand-to-mouth events is based on Xue et al, 2007. The estimates of mouthing frequency were derived from several exposure studies and videotaping studies. Statistical analysis indicated that a Weibull distribution best fit the data. For the lawn care scenario, hand-to-mouth events per hour were based on outdoor frequencies as defined by a Weibull distribution (mean = 6 events/hour, standard deviation = 8). OPP believes that the meta-analysis cited above provides the best available data to assess children's hand-to-mouth exposures.

Surface Area of Hand Mouthed: The revised NMC CRA relied on Zartarian's (2003) analysis of surface area of hand mouthed. The analysis used the Leckie, et al., 2000 data to determine the fraction of the hand mouthed. The fraction of hand mouthed values were fit with a beta distribution (mean = 0.13 events/hour, standard deviation = 0.06).

Saliva Extraction Factor: To address the removal of residues from the hands by saliva during mouthing events, several studies were considered. The removal efficiency of residues on hands by saliva and



other substances (e.g., ethanol) suggests a range of removal efficiencies (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989). Based on the above studies, a uniform distribution of 20% to 50% was used in this assessment for saliva extraction factors.

Duration: The time spent on the lawn was estimated as a cumulative distribution ranging from 0 hours to 3.5 hours. To be protective of childrens' exposure and to address the uncertainty of the upper percentiles of the exposure factor data, OPP selected a cumulative distribution from EFH (USEPA, 1997a) Table 15-80 with a bound of 3.5 hours for children 1 to 5 years old. This distribution represents the amount of time spent outdoors. This allows for the time that children spend outdoors not only at home but also in parks and near schools.

Assessing exposure through the non-dietary ingestion pathway is difficult due, in part, to issues associated with measurement of the above-discussed variables as well as issues associated with the utility of using children's hand-to-mouth frequencies based on indoor activities for outdoor exposure scenarios. There are also differences in mouthing behavior based on active and quiet play with increased mouthing likely to be during activities of quiet play. Limited data evaluated by Groot et al., 1998 suggests that children aged six to 12 months can experience longer durations of mouthing activities (exceeding 160 minutes per day) than children 18 to 36 months (up to 30 minutes per day). However, children in this age group are not likely to be engaged in post-application lawn activities OPP is modeling that would result in higher estimated exposure. Additional data for very young children (under the age of two) are needed to delineate the frequency differences between hand-to-mouth events for children engaged in active and quiet play.

b. Vegetable Garden Exposure Scenarios

Carbaryl has registered uses in home vegetable gardens. This assessment includes scenarios for applications of carbaryl using dust formulations (hand/shake), ready-to-use trigger sprayers, and hose-end sprayers. While there are other possible application methods for use on these sites, these application methods were selected based on use and exposure considerations.

i. Applicator Exposure

Dermal and inhalation exposures for homeowners applying carbaryl to their vegetable gardens were calculated in a manner similar to that used to assess applicator exposure for the lawn care scenario. Both are the product of the unit exposure (mg/lb ai handled), application rate (lbs ai/ft²), and area treated (ft²).



Unit Exposure: Dermal and inhalation unit exposures were derived from chemical-specific data (Mester, 1998a) for dust (shake/pour), trigger pump sprayer, and liquid hose-end sprayer applications to vegetable gardens. The UE for all garden scenarios are based on lognormal distribution as listed in [REF _Ref177472796 \h].

Application Rate: An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lb ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lbs ai/container (see Table II.A). The exposure assessment for dust formulation applied to home gardens assumes use of one entire container per treatment.

Area Treated: For vegetable gardens, the area treated was entered as a lognormal distribution (mean = 4600 ft², standard deviation = 1500 ft², and maximum = 8000 ft²); these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999). In these assessments, it is assumed that the entire garden is treated. Home gardens consist of many types of vegetables which all may not be treated since they tend to have different pest pressures (e.g. squash vine borer and corn earworm may not appear at the same time).

Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Lognormal Distributions of Unit Exposures Used for Carbaryl Garden, Fruit Tree, and Ornamental Scenarios

Application Method	Exposure Route	Unit Exposure Distribution(mg/lb ai)	Comments
Hose-End Sprayer	Dermal	(51, 58)	This distribution used for the vegetable garden scenario ONLY
	Inhalation	(0.0024, 0.0015)	
Liquid Handwand	Dermal	(74, 64)	This distribution also used for the ornamental and fruit tree scenarios
	Inhalation	(0.009, 0.010)	
Dust Shaker/Powder	Dermal	(250, 330)	This distribution was used for vegetable garden and ornamental scenarios. This distribution was also used for the SPOT treatment on lawns.
	Inhalation	(2.9, 9.5)	
RTU Trigger Pump Sprayer	Dermal	(86, 110)	This distribution was used for the vegetable garden and ornamental scenarios.
	Inhalation	(0.10, 0.14)	

NOTES: LN(μ , σ) represents a lognormal distribution with μ = mean and σ = standard deviation
 Studies for garden, fruit tree, and ornamental applications are carbaryl-specific.
 A more detailed explanation of the statistical analysis of this data is provided in Appendix II.D.2.



ii. *Post-Application Dermal Exposure*

Post-application exposure for adults and teenagers harvesting vegetables or performing post-application gardens maintenance were assessed using a range of transfer coefficients to account for the diversity of activities. Post-application exposure was estimated as the product of dislodgeable residue concentration (mg/cm^2) a transfer coefficient (cm^2/hour), and time spent in the activity (hours).

Residue Data: Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a) , the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. Statistical analysis of the carbaryl sunflower DFR data was performed. The initial residue concentrations and the half-life were determined to be $0.0061 \text{ mg}/\text{cm}^2$ and 5 days, respectively.

Transfer Coefficient: For the vegetable garden scenario, transfer coefficients were characterized by a uniform distribution ranging from 180 to $1000 \text{ cm}^2/\text{hour}$, to reflect a range of gardening tasks for a variety of crops of differing heights and foliage development. The TCs used in this assessment were derived from studies on chrysanthemum pinching (Rotondaro, 2000) and tomato harvesting (USEPA, 2000e). All transfer coefficients are based on individuals wearing short sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.

Duration: The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).

c. **Ornamental Plants and Shrubs Exposure Scenarios**

Carbaryl also has registered uses on ornamental plants and shrubs. This assessment includes scenarios for the RTU dust formulations, RTU trigger pump sprayers, and liquid hand wand uses on ornamental plants. While there are other possible application methods for use on this site, these methods were selected based on use and exposure considerations.



i. Applicator Exposure

Dermal and inhalation exposures for homeowners treating ornamental plants were estimated as the product of the Unit Exposure (mg/lb ai handled), application rate (lbs ai/ft²), and area treated (ft²).

Unit Exposure: Dermal and inhalation unit exposures were derived from chemical-specific data for carbaryl used on ornamental plants (Mester, 1998a; Merricks, 1998). The UE for all garden scenarios are based on lognormal distribution as listed in Table I.D.3.

Application Rate: An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lbs ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lb ai/container. The exposure assessment for dust formulation applied to ornamental gardens assumes use of one entire container per treatment.

Area Treated: The area treated was entered as a uniform distribution of 500 to 2000 ft²; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The ornamental bed size was determined by estimating the perimeter of 2200 ft² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.

ii. Post-Application Dermal Exposure

Post-application exposure for adults and teenagers performing ornamental garden activities were assessed using a range of transfer coefficients to account for the diversity of activities. Post-application exposure was estimated as the product of dislodgeable residue concentration (mg/ cm²), transfer coefficient (cm²/hour), and time spent in the activity (hours).

Residue Data: Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure from harvesting or performing maintenance activities in ornamental gardens. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a), the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. A statistical analysis of this data was performed and the



initial concentration was estimated to be 0.0061 mg/ cm². Residue dissipation is based on the half-life of 5 days. The half-life used in this assessment was determined from the statistical analysis of the carbaryl sunflower DFR data. A more detailed explanation of the statistical analysis of this data is provided in Appendix II.D.2.

Transfer Coefficient: For the ornamental garden scenario, a uniform distribution of transfer coefficients, ranging from 99 to 550 cm²/hour, was used to reflect a range of gardening tasks. The TCs used in this assessment were derived from studies that evaluated chrysanthemum pinching (Rotondaro, 2000) and nursery stock pruning (Klone et al, 2000b). All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.

Duration: The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post-application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).

d. Fruit Tree Exposure Scenarios

Carbaryl also has registered uses on fruit trees. This assessment addresses exposure for homeowners applying sprayable formulations of carbaryl via handwands. While there are other possible application methods for use on these sites, this method was selected based on use and exposure considerations.

i. Applicator Exposure

As described for the lawn applicator scenario, exposure is the product of the unit exposure (mg/lb ai handled), application rate (lbs ai/ft²), and area treated (ft²).

Unit Exposure: The dermal and inhalation unit exposures were derived from chemical-specific data for liquid handwand applications to fruit trees (Merricks, 1998). These unit exposures are based on study data in which applications were made with handwands, spraying below the waist as well as overhead. The UEs for fruit tree scenario are based on lognormal distribution as listed in Table I.D.3.



Application Rate: For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the fruit tree scenario).

Area Treated: For fruit trees, most of which are of the dwarf variety and therefore occupy relatively small areas, the area treated was entered as a uniform distribution (minimum 500 ft², maximum 1000 ft²). The maximum value in this distribution was based on label restriction for applications made at the maximum rate (8lbs ai/A) for fruit tree applications.

ii. *Post-Application Dermal Exposure*

Dermal post-application exposure for adults and teenagers harvesting or pruning fruit trees was assessed using TCs from an apple pruning study. Post- application exposure was estimated as the product of dislodgeable residue concentration (mg/ cm²), transfer coefficient (cm²/hour), and time spent in the activity (hours).

Residue Data: Chemical specific dislodgeable foliar residue data on olive trees (Klone et al, 2000c) were used to assess dermal post-application exposure for this scenario. Statistical analysis of this data was performed and the initial residue concentrations were determined to be 0.0035 mg/ cm². Residue dissipation is based on the half-life of 7 days (as determined by the statistical analysis of the carbaryl olive DFR data).

Transfer Coefficient: For the fruit tree scenario, the distribution of transfer coefficient was characterized as lognormal, with a mean of 940 cm²/hour and a standard deviation of 260 cm²/hour. The TCs were based on an apple pruning study. All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.

Duration: The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).

e. **Ornamental Garden - Snail and Slug Bait Scenarios**

This assessment includes the bait use of methiocarb in ornamental gardens. Applicator exposure is calculated as the product of the unit exposure (mg/lb ai handled), application rate (lbs ai/ft²), and area treated (ft²).



i. Applicator Exposure

Unit Exposure: The dermal and inhalation UEs for the methiocarb snail and slug bait scenario were based on study data for disulfoton applications to residential shrubs and flower beds (Merricks, 2001). The surrogate data consist of dermal and inhalation measurements of individuals using granular products. Specifically, the field study was conducted in Vero Beach, Florida. A total of 15 volunteers were monitored using passive dosimetry (hand/forearm wash solutions and personal air monitors). Application of the product was made by pouring the granules into the measuring cup/lid attached to the product package, and then distributing the granules onto the soil around the base of a shrub or onto a flower bed. The granules were then soil-incorporated with a garden rake. Each volunteer applied granular disulfoton around shrubs while wearing gloves and then again without gloves. Exposure data from the 15 replicates who did not wear gloves were reported. A lognormal distribution with a mean of 0.23 mg/lb ai, a standard deviation of 5.8 mg/lb ai, and maximum value of 3.4 mg/lb ai (representing the estimated 99th percentile of the lognormal distribution) was used to assess dermal exposure. A single point estimate of 0.00001 mg/lb ai (1/2 LOQ) was used for the inhalation UE since all measured values for inhalation were non-detects.

Application Rate: The application rate used in this assessment is based on the maximum label application rate of 0.2 lbs ai/1000 ft².

Area Treated: The area treated was entered as a uniform distribution of 10 to 2000 ft²; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The low value of 10 sq ft was based on the label direction for treating small areas. The high value for ornamental bed size was determined by estimating the perimeter of 2200 ft² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.

ii. Post-Application Exposure

Since this product is formulated as a bait and is applied as a broadcast application over plant foliage or to the soil surrounding ornamental plants, post-application exposure is expected to be minimal in comparison to the post-application exposure assessed for the ornamental use of carbaryl. Therefore, post-application exposure was not evaluated for the methiocarb snail and slug bait scenario.



f. Pet Collar Scenarios

The revised NMC CRA also considered exposures through the use of flea collar products for carbaryl and propoxur. These assessments rely on Agency default assumptions for pet fur transferable residues. The dermal contact factor(s) for post-application exposure is based on a shampoo and groomer exposure study for carbaryl (each groomer shampooed, brushed and groomed 8 dogs) (Mester, 1998b). Each groomer shampooed the dogs, picked them up wet to be placed in crates until all the dogs were shampooed. The dogs were then dried and groomed. These activities are likely to result in higher contact factors than intermittent contact with a pet wearing a collar.

i. Applicator Exposure

Applicator exposure was not directly considered in this assessment since it is expected to be minimal when compared to the post-application exposure.

ii. Post-Application Dermal Exposure

Post-application dermal exposure scenarios were considered for both adults and children while post-application non-dietary oral exposure scenarios (oral hand-to-mouth) were assumed to apply only to children ages 1-5 years old. These data, as described below, were used to assess the pet collar uses of both carbaryl and propoxur. Frequency, timing, and probability of collar treatments are also incorporated in the revised NMC CRA.

Dermal post-application exposure (to adults and children) was calculated as the product of residue concentration (mg/cm^2), the transfer coefficient (in cm^2/hour), and the duration of exposure (hours/day). A further description of each of these terms is presented below:

Residue Concentration: The fur residue concentration for the pet collar assessment is based on the amount of active ingredient in the respective pet collars and Agency default assumptions from the OPP Standard Operating Procedures (SOPs) for Residential Exposure Assessment (USEPA, 1997b). The residue values for carbaryl and propoxur are 0.00012 and 0.000069 mg/cm^2 , respectively. Residues were assumed to be available on a daily basis since pet collar products are designed to emit residues throughout their active period (120 days for carbaryl and 180 days for propoxur).

Transfer Coefficient: The transfer coefficients used in the dermal post-application exposure assessment were derived from a groomer



exposure study (Mester, 1998b) in which sixteen different veterinary personnel treated/handled eight dogs each, over a two to five hour time period. In this assessment, the transfer coefficients for adults and children were derived assuming an average transfer efficiency of 2.97% from the previous OP pet fur residue transfer efficiencies. For the revised NMC CRA, the data were used directly to generate an empirical distribution for the dermal transfer coefficient. The selected TCs ranged from 180 to 4700 cm²/hour for adults and from 66 to 1800 cm²/hour for children. These empirical distributions were used for both pet collar scenarios.

Duration: The time spent in this activity was assumed to follow a triangular distribution with a minimum value of 0.03 hours and a maximum value of 1.03 hours per day (Freeman et al, 2001). As part of this study, macroactivity and microactivity data were collected via questionnaires and videotaping of 19 children (aged 3 to 12) for a four hour period. The videotapes from the observational portion of this study were analyzed to determine frequency of contacts for several mouthing behaviors, as well as duration of time each child spent in various locations around the home. The results of this study include several measurements for the duration of time the observed children spent with their pets.

In this assessment, the duration of exposure is assumed to be continuous contact rather than the intermittent contact normally associated with pet care (e.g. walking, feeding). Furthermore, dog collar residues are likely to be localized around the neck, and therefore, contact with other areas of the pet will result in little to no exposure. OPP is attempting to draw the distinction between direct contact with a treated pet and the time spent with a pet where there is limited contact. For example, time spent with pets in and around the house or sleeping in the same bed may not result in direct contact for the entire duration. The pet collar scenario assessed in the revised NMC CRA uses pet fur residues transferred to individuals at a rate found during a study of shampooing and grooming, for a duration of approximately 1 hour. Use of these data to represent residential exposure to pets is likely to encompass all other potential exposure scenarios involving direct or indirect contact with treated pets.

iii. Oral (Hand-to-Mouth) Post-Application Exposure

Post-application exposure through the oral (hand-to-mouth) route was also assessed for children ages 1-5 using the approach detailed in Section I.D.4.i of this document.



The approach taken to assess hand-to-mouth exposure is the same as that used to assess the lawn scenario oral non-dietary exposure. The initial hand loading values were determined as a portion of total dermal exposure variable to the hands. Additionally, contact factors, fraction of surface area of hand mouthed (Zartarian, 2003), saliva extraction factor (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989)) are the same as those used in the lawn care assessment. The estimates of mouthing frequency were derived from several exposure studies and videotaping studies. For the pet collar scenario, hand-to-mouth events per hour were based on indoor frequencies as defined by a Weibull distribution (mean = 13 events/hour, standard deviation = 18). The distribution for frequency of hand-to-mouth events for indoor exposures, (provided by ORD's Dr. Jiaping Xue), was calculated based on the same methodology for outdoor exposures in the lawn care assessment. OPP believes that this analysis provides the best available data to assess children's hand-to-mouth exposures. The duration of exposure values used for the non-dietary exposure assessment are the same as those used in the dermal post-application assessment for the pet collar scenarios presented above.

g. Golf Course Scenario

i. *Post-Application Dermal Exposure*

Carbaryl is also used on golf courses. The current assessment addresses dermal post-application exposure for adults and teens playing rounds of golf on treated courses. Post-application exposure was estimated as the product of turf-transferable residue (mg/cm^2), transfer coefficient (cm^2/hour), and time spent in the activity (hours).

The percent of the population playing golf and the percent of golf courses that are treated with carbaryl was also considered and incorporated into the assessment. The 1992 Golf Course Operations: Cost of Doing Business/Profitability survey conducted by the Center for Golf Course Management (CGCM) was used to establish the percent of individuals playing golf. The CGCM survey reported that an average of 12% of the population plays golf. To determine the likelihood of playing golf on a treated golf course, percent of golf courses treated data provided by Doane's GolfTrak (1998-1999) were used. These data indicated up to 25% of golf courses are treated with carbaryl, depending upon the region of use.

Residue Data: Since liquid broadcast applications to golf course turf are permitted, the liquid TTR data (Mester, 1999) were used to assess post-application exposure for the golf course scenario. Statistical analysis of these data was performed and an initial concentration of



0.00065 mg/ cm² was calculated and used in this assessment. Dissipation is based on a 3.6 day half-life. For details of the statistical analysis see Appendix II.D.2.

Transfer Coefficients: The surrogate data used to derive transfer coefficients were based on two measurements of four individuals playing golf on two golf courses treated with chlorothalonil (Ballee, 1990), and the exposure of golfers (four volunteers) to flurprimidol (Moran et al, 1987). For both studies, an assumed transfer efficiency of 1% was used to calculate the transfer coefficients, since the studies were conducted using sprayable formulations. Based on these two studies, a lognormal distribution with a mean of 480 cm²/hour and a standard deviation of 160 cm²/hour was used to represent the transfer coefficient. This distribution was truncated at the calculated 99th percentile value of 960 cm²/hour. All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weight and surface area differences for adults and teenagers.

Duration: The exposure duration for individuals playing golf was assumed to be a uniform distribution bounded at the low end by two hours and at the upper end at four hours. The four-hour value was obtained from the CGCM survey.

7. Risk

For all subpopulations, the MOEs are greater than 10 when all uses are considered, at the 95th, 99th, and 99.9th percentiles. Graphs for all percentiles of regulation and all subpopulations are described in more detail in the cumulative chapter (F), of this document. (See Appendix III for detailed graphs.)

8. Summary

This assessment relied upon the best available data from all sources that could be identified. Sources included chemical specific and task force-generated data, as well as data from the scientific literature.

The revised NMC CRA assessment was performed for the Southeast region of the United States. While insect growth may slow during the winter months in the South, unlike other regions of the country, there is no period of dormancy. Since the growing season is longer in the South and the associated pest pressures are therefore greater, this assessment provides a worst case estimate of exposure. The residential assessment of the revised NMC CRA includes the carbaryl lawn and golf course use, the carbaryl vegetable and ornamental garden use, the methiocarb snail and slug bait use, the



carbaryl fruit tree use, and the carbaryl and propoxur pet collar uses. All MOEs are greater than 10 and therefore not of concern.



Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Summary of NMC Residential Exposure Scenarios

Lawn Care Scenario	
Applicator Exposure	
Unit Exposure	Both dermal and inhalation exposure routes were considered. ORETF studies were used for the granular broadcast and liquid spot treatment scenarios. The ORETF (Outdoor Residential Exposure Task Force) submitted a report (Klonne, 1999) in which a variety of products were used on turf. In these studies, both homeowners and lawn care operators (LCOs) were monitored following broadcast applications to turf. All of the data submitted in this report were completed in a series of studies. The two studies that monitored homeowner exposure resulting from granular spreader (Klonne, 1999/OMA003 Study) and hose-end sprayer (Klonne, 1999/OMA004 Study) applications were used in this assessment. Volunteers participating in these exposures studies were adult non-professionals who use pesticides on their own gardens and lawns. Many of the volunteers selected as subjects in these studies were members of garden clubs. All volunteers made their applications without specific instruction from the study investigators. Unit exposures estimated from these studies cover various clothing scenarios that range from wearing short pants and short-sleeved shirts, to long pants and long-sleeved shirts. All dermal and inhalation unit exposure were normalized and expressed as milligrams exposure per pound of active ingredient handled (mg/lb ai) (referred to as unit exposures, or UE). The lognormal distributions of the UEs for the lawn applicator scenarios are shown in Table I.D.2.
Application Rate	For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the lawn care scenario).
Area Treated	An important variable for estimating home-owner applicator exposure is the size of the lawn. OPP considered the average and median lawn sizes reported in a journal article by Vinlove and Torla (1995). The means and medians were ~13,000 ft ² . However, the authors noted problems interpreting the data since it is based primarily on low income houses and consists of adjustments of the lot size by the house's foundation (footprint) only. The data do not consider other structures such as decks or other green space such as gardens, which can reportedly reduce the lot size by up to 50%. Similar lawn sizes were noted in ORETF study (Johnson et al, 1999) with similar problems encountered with respect to confounding variables such as decks and other green spaces. For this assessment, OPP used a uniform distribution for lawn size bounded by 1000 ft ² and 20,000 ft ² . The lower end of this range considers smaller lawns for residences such as town houses. The upper bound of 20,000 ft ² (~ ½ acre) appears reasonable given the type of application equipment assumed to be used by residential applicators. Information from the ORETF survey also indicates that many pesticide users make spot treatments of insecticides. Similarly for spot treatments, OPP assumed a uniform distribution for treated area bounded by 100 ft ² and 1000 ft ² .
Dermal Post-Application Exposure	
Residue	There are chemical-specific turf transferable residue (TTR) data for granular formulations of carbaryl (Krolski, 2005). This study was designed to determine transferable residues of carbaryl from both irrigated and non-irrigated turf treated with SEVIN® 2G (see Appendix II.D.2 for study summary). Measured carbaryl residues rapidly declined over the first 4 hours and then leveled off or rose



	slightly after 12 hours. By the 24-hour sampling interval, the residues declined to approximately 10 percent of the corresponding 0-time residue value and then steadily dropped to below 1.0 percent of the corresponding 0-time residue values by 3- to 5-days after treatment. In order to provide a conservative estimate of exposure for the revised NMC CRA, only the samples from the non-irrigated site in Florida were used. This assessment assumes an initial concentration of 0.00021 mg/ cm ² . Dissipation is based on a 0.8 day half-life, with residues set to zero 14 days after application. Although the carbaryl TTR studies show residues below 1% of the initial residues by 3- to 5-days after application, to provide a conservative estimate of exposure, it is assumed that carbaryl residues on the lawn would be available for up to 2 weeks after application.
TC	<p><u>Transfer Coefficients used to assess children's exposure to treated turf:</u></p> <p>One study was used to assess children's dermal exposure resulting from granular applications to residential turf (Vaccaro, 1996). In this study, a granular formulation of chlorpyrifos was applied, after which seven adults performed pre-choreographed activities intended to mimic a typical child's behavior. The subjects performed these activities for a period of four hours beginning after the turf had dried. Turf had been treated earlier with a granular form of chlorpyrifos and exposure was estimated in the study by monitoring the amount of a chlorpyrifos metabolite – 3,4,5, 6-TCP – excreted over the following period of 6 days. This method directly measures internal dose and was used to back-calculate a generic "to the skin" transfer coefficient by using chemical specific dermal absorption data for chlorpyrifos (Nolan et al, 1984). These data were further adjusted to account for differences in surface area of adults and children. The study data discussed above was fit to a lognormal distribution with an arithmetic mean of 1970 cm²/hr with a standard deviation of 1426 cm²/hr. The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e. 7224 cm²/hr for the granular application) in order to avoid a distribution which contained values that were well-beyond those that are deemed reasonable. (see Appendix II.D.2 for study summary and details of the distributional analysis).</p> <p><u>Transfer Coefficients used to assess adult exposure to treated turf:</u></p> <p>The Vaccaro study data discussed above were also used to assess exposure to adults following granular applications. The revised NMC CRA used a distribution of values for the transfer coefficient characterized by a lognormal distribution with an arithmetic mean, of 5376 cm²/hr and a standard deviation of 4717 cm²/hr for the granular application. The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e. 23436 cm²/hr for the granular application. See Appendix II.D.2 for study summary and details of the distributional analysis).</p>
Duration	Another important variable for addressing post-application exposure from home lawn treatment is the duration of time spent on lawns. In this revised NMC CRA, cumulative distributions of durations on lawns of up to two hours were used to address adult exposure on lawns. These data are presented in Table 15-64 of the EPA's Exposure Factor's Handbook (EFH) (USEPA, 1997a); however, OPP notes that the percentiles above the 95th have the same values (121 minutes). A similar cumulative distribution was given for children ages one to five. In order to be protective of children and to address the uncertainty in the upper percentiles of the exposure factor data, OPP selected an empirical distribution (which was expressed as a cumulative distribution function) from EFH Table 15-80 with a bound of 3.5 hours for children (USEPA, 1997a). This distribution represents the amount of time spent outdoors rather than just on lawns. This adjustment allows for additional time that children may spend outdoors (such as parks and schools) where there is potential for additional contact with treated turf.
Oral non-dietary Post-Application Exposure	
Initial Hand Loadings	Hand loading (HR/2) is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA EFH indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over (USEPA, 2002c). The algorithm assumes mouthing one hand at a time, therefore, hand loading residues are divided by 2.



Frequency of mouthing events	For the revised NMC CRA assessment, the frequency of hand-to-mouth events is based on Xue et al, 2007. The estimates of mouthing frequency were derived from several exposure studies and videotaping studies. Statistical analysis indicated that a Weibull distribution best fit the data. For the lawn care scenario, hand-to-mouth events per hour were based on outdoor frequencies as defined by a Weibull distribution (mean = 6 events/hour, standard deviation = 8). OPP believes that the meta-analysis cited above provides the best available data to assess children's hand-to-mouth exposures.
Surface Area Mouthed	The revised NMC CRA relied on Zartarian's (2003) analysis of surface area of hand mouthed. The analysis used the Leckie, et al, 2000 data to determine the fraction of the hand mouthed. The fraction of hand mouthed values were fit with a beta distribution (mean = 0.13 events/hour, standard deviation = 0.06).
Saliva Extraction Factor	To address the removal of residues from the hands by saliva during mouthing events, several studies were considered. The removal efficiency of residues on hands by saliva and other substances (e.g., ethanol) suggests a range of removal efficiencies (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989). Based on the above studies, a uniform distribution of 20% to 50% was used in this assessment for saliva extraction factors.
Duration	The time spent on the lawn was estimated as a cumulative distribution ranging from 0 hours to 3.5 hours. To be protective of childrens' exposure and to address the uncertainty of the upper percentiles of the exposure factor data, OPP selected a cumulative distribution from EFH (USEPA, 1997a) Table 15-80 with a bound of 3.5 hours for children 1 to 5 years old. This distribution represents the amount of time spent outdoors. This allows for the time that children spend outdoors not only at home but also in parks and near schools.
Vegetable Garden Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	Dermal and inhalation unit exposures were derived from chemical-specific data (Mester, 1998a) for dust (shake/pour), trigger pump sprayer, and liquid hose-end sprayer applications to vegetable gardens. The UE for all garden scenarios are based on lognormal distribution as listed in Table I.D.3.
Application Rate	An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lb ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lbs ai/container (see Table I.A). The exposure assessment for dust formulation applied to home gardens assumes use of one entire container per treatment.
Area Treated	For vegetable gardens, the area treated was entered as a lognormal distribution (mean = 4600 ft ² , standard deviation =1500 ft ² , and Taximum = 8000 ft ²); these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999). In these assessments, it is assumed that the entire garden is treated. Home gardens consist of many types of vegetables which all may not be treated since they tend to have different pest pressures (e.g. squash vine borer and corn earworm may not appear at the same time).
Dermal Post-Application Exposure	
Residue	Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a), the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. Statistical analysis of the carbaryl sunflower DFR data was performed. The initial residue concentrations and the half-life were determined to be 0.0061 mg/ cm ² and 5 days, respectively.



TC	For the vegetable garden scenario, transfer coefficients were characterized by a uniform distribution ranging from 180 to 1000 cm ² /hour, to reflect a range of gardening tasks for a variety of crops of differing heights and foliage development. The TCs used in this assessment were derived from studies on chrysanthemum pinching (Rotondaro, 2000) and tomato harvesting (USEPA, 2000e). All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.
Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Ornamental Plants and Shrub Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	Dermal and inhalation unit exposures were derived from chemical-specific data for carbaryl used on ornamental plants (Mester, 1998a; Merricks, 1998). The UE for all garden scenarios are based on lognormal distribution as listed in Table I.D.3.
Application Rate	An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lb ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lbs ai/container (see Table II.A). The exposure assessment for dust formulation applied to ornamental gardens assumes use of one entire container per treatment.
Area Treated	The area treated was entered as a uniform distribution of 500 to 2000 ft ² ; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The ornamental bed size was determined by estimating the perimeter of 2200 ft ² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.
Dermal Post-Application Exposure	
Residue	Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure from harvesting or performing maintenance activities in ornamental gardens. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a), the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. A statistical analysis of this data was performed and the initial concentration was estimated to be 0.0061 mg/ cm ² . Residue dissipation is based on the half-life of 5 days. The half-life used in this assessment was determined from the statistical analysis of the carbaryl sunflower DFR data. A more detailed explanation of the statistical analysis of this data is provided in Appendix II.D.2.
TC	For the ornamental garden scenario, a uniform distribution of transfer coefficients, ranging from 99 to 550 cm ² /hour, was used to reflect a range of gardening tasks. The TCs used in this assessment were derived from studies that evaluated chrysanthemum pinching (Rotondaro, 2000) and nursery stock pruning (Klonne et al, 2000b). All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.



Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post-application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Fruit Tree Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	The dermal and inhalation unit exposures were derived from chemical-specific data for liquid handwand applications to fruit trees (Merricks, 1998). These unit exposures are based on study data in which applications were made with handwands, spraying below the waist as well as overhead. The UEs for fruit tree scenario are based on lognormal distribution as listed in Table I.D.3.
Application Rate	For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the fruit tree scenario).
Area Treated	For fruit trees, most of which are of the dwarf variety and therefore occupy relatively small areas, the area treated was entered as a uniform distribution (minimum 500 ft ² , maximum 1000 ft ²). The maximum value in this distribution was based on label restriction for applications made at the maximum rate (8lbs ai/A) for fruit tree applications.
Dermal Post-Application Exposure	
Residue	Chemical specific dislodgeable foliar residue data on olive trees (Klonne et al, 2000c) were used to assess dermal post-application exposure for this scenario. Statistical analysis of this data was performed and the initial residue concentrations were determined to be 0.0035 mg/ cm ² . Residue dissipation is based on the half-life of 7 days (as determined by the statistical analysis of the carbaryl olive DFR data).
TC	For the fruit tree scenario, the distribution of transfer coefficient was characterized as lognormal, with a mean of 940 cm ² /hour and a standard deviation of 260 cm ² /hour. The TCs were based on an apple pruning study. All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.
Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post-application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Ornamental Garden - Snail and Slug Bait Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	The dermal and inhalation UEs for the methiocarb snail and slug bait scenario were based on study data for disulfoton applications to residential shrubs and flower beds (Merricks, 2001). The surrogate data consist of dermal and inhalation measurements of individuals using granular products. Specifically, the field study was conducted in Vero Beach, Florida. A total of 15 volunteers were monitored using passive dosimetry (hand/forearm wash solutions and personal air monitors). Application of the product was made by pouring the granules into the measuring cup/lid attached to the product package, and then distributing the granules onto



	the soil around the base of a shrub or onto a flower bed. The granules were then soil-incorporated with a garden rake. Each volunteer applied granular disulfoton around shrubs while wearing gloves and then again without gloves. Exposure data from the 15 replicates who did not wear gloves were reported. A lognormal distribution with a mean of 0.23 mg/lb ai, a standard deviation of 5.8 mg/lb ai, and maximum value of 3.4 mg/lb ai (representing the estimated 99th percentile of the lognormal distribution) was used to assess dermal exposure. A single point estimate of 0.00001 mg/lb ai (1/2 LOQ) was used for the inhalation UE since all measured values for inhalation were non-detects.
Application Rate	The application rate used in this assessment is based on the maximum label application rate of 0.2 lbs ai/1000 ft ² .
Area Treated	The area treated was entered as a uniform distribution of 10 to 2000 ft ² ; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The low value of 10 sq ft was based on the label direction for treating small areas. The high value for ornamental bed size was determined by estimating the perimeter of 2200 ft ² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.
Pet Collar Scenarios	
Dermal Post-Application Exposure	
Residue	The fur residue concentration for the pet collar assessment is based on the amount of active ingredient in the respective pet collars and Agency default assumptions from the OPP SOPs for Residential Exposure Assessment (USEPA, 1997b). The residue values for carbaryl and propoxur are 0.00012 and 0.000069 mg/ cm ² , respectively. Residues were assumed to be available on a daily basis since pet collar products are designed to emit residues throughout their active period (120 days for carbaryl and 180 days for propoxur).
TC	The transfer coefficients used in the dermal post-application exposure assessment was derived from a groomer exposure study (Mester, 1998b) in which sixteen different veterinary personnel treated/handled eight dogs each, over a two to five hour time period. In this assessment, the transfer coefficients for adults and children were derived assuming an average transfer efficiency of 2.97% from the previous OP pet fur residue transfer efficiencies. For the revised NMC CRA, the data were used directly to generate an empirical distribution for the dermal transfer coefficient. The selected TCs ranged from 180 to 4700 cm ² /hour for adults and from 66 to 1800 cm ² /hour for children. These empirical distributions were used for both pet collar scenarios.
Duration	The time spent in this activity was assumed to follow a triangular distribution with minimum value of 0.03 hours, and a maximum value of 1.03 hours per day (Freeman et al, 2001). As part of this study, macroactivity and microactivity data were collected via questionnaires and videotaping of 19 children (aged 3 to 12) for a four hour period. The videotapes from the observational portion of this study were analyzed to determine frequency of contacts for several mouthing behaviors, as well as duration of time each child spent in various locations around the home. The results of this study include several measurements for the duration of time the observed children spent with their pets.
Oral non-dietary Post-Application Exposure	
Initial Hand Loadings	Hand loading (HR/2) is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA Exposure Factors Handbook indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over (USEPA, 2002c). The algorithm assumes mouthing one hand at a time, therefore, hand loading residues are divided by 2.



Frequency of mouthing events	The estimates of mouthing frequency were derived from several exposure studies and observational studies. For the pet collar scenario, hand-to-mouth events per hour were based on indoor frequencies as defined by a Weibull distribution (mean = 13 events/hour, standard deviation = 18). The distribution for frequency of hand-to-mouth events for indoor exposures, provided by ORD's Dr. Jiaping Xue, was calculated using the same methodology used to determine the frequency of mouthing events for outdoor exposures that was used in the lawn care assessment.
Surface Area Mouthed	The revised NMC CRA relied on Zartarian's (2003) analysis of surface area of hand mouthed. The analysis used the Leckie, et al, 2000 data to determine the fraction of the hand mouthed. The fraction of hand mouthed values were fit with a beta distribution (mean = 0.13 events/hour, standard deviation = 0.06).
Saliva Extraction Factor	To address the removal of residues from the hands by saliva during mouthing events, several studies were considered. The removal efficiency of residues on hands by saliva and other substances (e.g., ethanol) suggests a range of removal efficiencies (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989). Based on the above studies, a uniform distribution of 20% to 50% was used in this assessment for saliva extraction factors.
Duration	The duration of exposure values used for the non-dietary exposure assessment are the same as those used in the dermal post-application assessment for the pet collar scenarios presented above.
Golf Course Scenario	
Dermal Post-Application Exposure	
Residue	Since liquid broadcast applications to golf course turf are permitted, the liquid TTR data (Mester, 1999) used to assess post-application exposure for the golf course scenario. Statistical analysis of this data was performed and an initial concentration of 0.00065 mg/ cm ² was calculated and used in this assessment. Dissipation is based on a 3.6 day half-life. For details of the statistical analysis see Appendix II.D.2.
TC	The surrogate data used to derive transfer coefficients were based on two measurements of four individuals playing golf on two golf courses treated with chlorothalonil (Ballee, 1990), and the exposure of golfers (four volunteers) to flurprimidol (Moran et al, 1987). For both studies, an assumed transfer efficiency of 1% was used to calculate the transfer coefficients, since the studies were conducted using sprayable formulations. Based on these two studies, a lognormal distribution with a mean of 480 cm ² /hour and a standard deviation of 160 cm ² /hour was used to represent the transfer coefficient. This distribution was truncated at the calculated 99th percentile value of 960 cm ² /hour. All transfer coefficients are based on individuals wearing short sleeved shirts and short pants. A reduction factor was applied to account for body weight and surface area differences for adults and teenagers.
Duration	The exposure duration for individuals playing golf was assumed to be a uniform distribution bounded at the low end by two hours and at the upper end at four hours. The four-hour value was obtained from the CGCM survey.
Applicator Exposure	



Unit Exposure	Both dermal and inhalation exposure routes were considered. ORETF studies were used for the granular broadcast and liquid spot treatment scenarios. The ORETF (Outdoor Residential Exposure Task Force) submitted a report (Klonne, 1999) in which a variety of products were used on turf. In these studies, both homeowners and lawn care operators (LCOs) were monitored following broadcast applications to turf. All of the data submitted in this report were completed in a series of studies. The two studies that monitored homeowner exposure resulting from granular spreader (Klonne, 1999/OMA003 Study) and hose-end sprayer (Klonne, 1999/OMA004 Study) applications were used in this assessment. Volunteers participating in these exposures studies were adult non-professionals who use pesticides on their own gardens and lawns. Many of the volunteers selected as subjects in these studies were members of garden clubs. All volunteers made their applications without specific instruction from the study investigators. Unit exposures estimated from these studies cover various clothing scenarios that range from wearing short pants and short-sleeved shirts, to long pants and long-sleeved shirts. All dermal and inhalation unit exposure were normalized and expressed as milligrams exposure per pound of active ingredient handled (mg/lb ai) (referred to as unit exposures, or UE). The lognormal distributions of the UEs for the lawn applicator scenarios are shown in Table I.D.2.
Application Rate	For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the lawn care scenario).
Area Treated	An important variable for estimating home-owner applicator exposure is the size of the lawn. OPP considered the average and median lawn sizes reported in a journal article by Vinlove and Torla (1995). The means and medians were ~13,000 ft ² . However, the authors noted problems interpreting the data since it is based primarily on low income houses and consists of adjustments of the lot size by the house's foundation (footprint) only. The data do not consider other structures such as decks or other green space such as gardens, which can reportedly reduce the lot size by up to 50%. Similar lawn sizes were noted in ORETF study (Johnson et al, 1999) with similar problems encountered with respect to confounding variables such as decks and other green spaces. For this assessment, OPP used a uniform distribution for lawn size bounded by 1000 ft ² and 20,000 ft ² . The lower end of this range considers smaller lawns for residences such as town houses. The upper bound of 20,000 ft ² (~ ½ acre) appears reasonable given the type of application equipment assumed to be used by residential applicators. Information from the ORETF survey also indicates that many pesticide users make spot treatments of insecticides. Similarly for spot treatments, OPP assumed a uniform distribution for treated area bounded by 100 ft ² and 1000 ft ² .
Dermal Post-Application Exposure	
Residue	There are chemical-specific turf transferable residue (TTR) data for granular formulations of carbaryl (Krolski, 2005). This study was designed to determine transferable residues of carbaryl from both irrigated and non-irrigated turf treated with SEVIN® 2G (see Appendix II.D.2 for study summary). Measured carbaryl residues rapidly declined over the first 4 hours and then leveled off or rose slightly after 12 hours. By the 24-hour sampling interval, the residues declined to approximately 10 percent of the corresponding 0-time residue value and then steadily dropped to below 1.0 percent of the corresponding 0-time residue values by 3- to 5-days after treatment. In order to provide a conservative estimate of exposure for the revised NMC CRA, only the samples from the non-irrigated site in Florida were used. This assessment assumes an initial concentration of 0.00021 mg/ cm ² . Dissipation is based on a 0.8 day half-life, with residues set to zero 14 days after application. Although the carbaryl TTR studies show residues below 1% of the initial residues by 3- to 5-days after application, to provide a conservative estimate of exposure, it is assumed that carbaryl residues on the lawn would be available for up to 2 weeks after application.



TC	<p><u>Transfer Coefficients used to assess children's exposure to treated turf:</u> One study was used to assess children's dermal exposure resulting from granular applications to residential turf (Vaccaro, 1996). In this study, a granular formulation of chlorpyrifos was applied, after which seven adults performed pre-choreographed activities intended to mimic a typical child's behavior. The subjects performed these activities for a period of four hours beginning after the turf had dried. Turf had been treated earlier with a granular form of chlorpyrifos and exposure was estimated in the study by monitoring the amount of a chlorpyrifos metabolite – 3,4,5, 6-TCP – excreted over the following period of 6 days. This method directly measures internal dose and was used to back-calculate a generic "to the skin" transfer coefficient by using chemical specific dermal absorption data for chlorpyrifos (Nolan et al, 1984). These data were further adjusted to account for differences in surface area of adults and children. The study data discussed above was fit to a lognormal distribution with an arithmetic mean of 1970 cm²/hr with a standard deviation of 1426 cm²/hr. The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e. 7224 cm²/hr for the granular application) in order to avoid a distribution which contained values that were well-beyond those that are deemed reasonable. (See Appendix II.D.2 for study summary and details of the distributional analysis.)</p> <p><u>Transfer Coefficients used to assess adult exposure to treated turf:</u> The Vaccaro study data discussed above were also used to assess exposure to adults following granular applications. The revised NMC CRA used a distribution of values for the transfer coefficient characterized by a lognormal distribution with an arithmetic mean, of 5376 cm²/hr and a standard deviation of 4717 cm²/hr for the granular application. The lognormal distribution was truncated at the calculated 99th percentile of the distribution (i.e. 23436 cm²/hr for the granular application). (See Appendix II.D.2 for study summary and details of the distributional analysis.)</p>
Duration	<p>Another important variable for addressing post-application exposure from home lawn treatment is the duration of time spent on lawns. In this revised NMC CRA, cumulative distributions of durations on lawns of up to two hours were used to address adult exposure on lawns. These data are presented in Table 15-64 of the EPA's Exposure Factor's Handbook (EFH) (USEPA, 1997a); however, OPP notes that the percentiles above the 95th have the same values (121 minutes). A similar cumulative distribution was given for children ages one to five. In order to be protective of children and to address the uncertainty in the upper percentiles of the exposure factor data, OPP selected an empirical distribution (which was expressed as a cumulative distribution function) from EFH Table 15-80 with a bound of 3.5 hours for children (USEPA, 1997a). This distribution represents the amount of time spent outdoors rather than just on lawns. This adjustment allows for additional time that children may spend outdoors (such as parks and schools) where there is potential for additional contact with treated turf.</p>
Oral non-dietary Post-Application Exposure	
Initial Hand Loadings	<p>Hand loading (HR/2) is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA EFH indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over (USEPA, 2002c). The algorithm assumes mouthing one hand at a time, therefore, hand loading residues are divided by 2.</p>
Frequency of mouthing events	<p>For the revised NMC CRA assessment, the frequency of hand-to-mouth events is based on Xue et al, 2007. The estimates of mouthing frequency were derived from several exposure studies and videotaping studies. Statistical analysis indicated that a Weibull distribution best fit the data. For the lawn care scenario, hand-to-mouth events per hour were based on outdoor frequencies as defined by a Weibull distribution (mean = 6 events/hour, standard deviation = 8). OPP believes that the meta-analysis cited above provides the best available data to assess children's hand-to-mouth exposures.</p>



Surface Area Mouthed	The revised NMC CRA relied on Zartarian's (2003) analysis of surface area of hand mouthed. The analysis used the Leckie, et al, 2000 data to determine the fraction of the hand mouthed. The fraction of hand mouthed values were fit with a beta distribution (mean = 0.13 events/hour, standard deviation = 0.06).
Saliva Extraction Factor	To address the removal of residues from the hands by saliva during mouthing events, several studies were considered. The removal efficiency of residues on hands by saliva and other substances (e.g., ethanol) suggests a range of removal efficiencies (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989). Based on the above studies, a uniform distribution of 20% to 50% was used in this assessment for saliva extraction factors.
Duration	The time spent on the lawn was estimated as a cumulative distribution ranging from 0 hours to 3.5 hours. To be protective of childrens' exposure and to address the uncertainty of the upper percentiles of the exposure factor data, OPP selected a cumulative distribution from EFH (USEPA, 1997a) Table 15-80 with a bound of 3.5 hours for children 1 to 5 years old. This distribution represents the amount of time spent outdoors. This allows for the time that children spend outdoors not only at home but also in parks and near schools.
Vegetable Garden Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	Dermal and inhalation unit exposures were derived from chemical-specific data (Mester, 1998a) for dust (shake/pour), trigger pump sprayer, and liquid hose-end sprayer applications to vegetable gardens. The UE for all garden scenarios are based on lognormal distribution as listed in Table I.D.3.
Application Rate	An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lb ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lbs ai/container. The exposure assessment for dust formulation applied to home gardens assumes use of one entire container per treatment.
Area Treated	For vegetable gardens, the area treated was entered as a lognormal distribution (mean = 4600 ft ² , standard deviation =1500 ft ² , and maximum = 8000 ft ²); these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999). In these assessments, it is assumed that the entire garden is treated. Home gardens consist of many types of vegetables which all may not be treated since they tend to have different pest pressures (e.g. squash vine borer and corn earworm may not appear at the same time).
Dermal Post-Application Exposure	
Residue	Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a), the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. Statistical analysis of the carbaryl sunflower DFR data was performed. The initial residue concentrations and the half-life were determined to be 0.0061 mg/ cm ² and 5 days, respectively.
TC	For the vegetable garden scenario, transfer coefficients were characterized by a uniform distribution ranging from 180 to 1000 cm ² /hour, to reflect a range of gardening tasks for a variety of crops of differing heights and foliage development. The TCs used in this assessment were derived from studies on chrysanthemum pinching (Rotondaro, 2000) and tomato harvesting (USEPA, 2000e). All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.



Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Ornamental Plants and Shrub Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	Dermal and inhalation unit exposures were derived from chemical-specific data for carbaryl used on ornamental plants (Mester, 1998a; Merricks, 1998). The UE for all garden scenarios are based on lognormal distribution as listed in Table I.D.3.
Application Rate	An application rate of 2 lbs ai/A was used for all liquid vegetable garden scenarios (hose-end sprayers and trigger pump sprayers) even though trigger pump sprayer rates are considerably lower. This assessment conservatively uses the 2 lb ai/A application rate for all liquid scenarios. Due to recent mitigation, the maximum application rate for dust formulations is 0.5 lbs ai/container. The exposure assessment for dust formulation applied to ornamental gardens assumes use of one entire container per treatment.
Area Treated	The area treated was entered as a uniform distribution of 500 to 2000 ft ² ; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The ornamental bed size was determined by estimating the perimeter of 2200 ft ² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.
Dermal Post-Application Exposure	
Residue	Chemical-specific dislodgeable foliar residue data on sunflowers (Klonne et al, 1999) were used to assess dermal post-application exposure from harvesting or performing maintenance activities in ornamental gardens. Although OPP has additional information regarding carbaryl specific DFR data on cabbage (Klonne et al, 2000a), the sunflower DFR data were used since the residues detected in the sunflower study were higher than those detected in the cabbage study. A statistical analysis of this data was performed and the initial concentration was estimated to be 0.0061 mg/ cm ² . Residue dissipation is based on the half-life of 5 days. The half-life used in this assessment was determined from the statistical analysis of the carbaryl sunflower DFR data. A more detailed explanation of the statistical analysis of this data is provided in Appendix II.D.2.
TC	For the ornamental garden scenario, a uniform distribution of transfer coefficients, ranging from 99 to 550 cm ² /hour, was used to reflect a range of gardening tasks. The TCs used in this assessment were derived from studies that evaluated chrysanthemum pinching (Rotondaro, 2000) and nursery stock pruning (Klonne et al, 2000b). All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.
Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Fruit Tree Scenario	



Dermal and Inhalation Applicator Exposure	
Unit Exposure	The dermal and inhalation unit exposures were derived from chemical-specific data for liquid handwand applications to fruit trees (Merricks, 1998). These unit exposures are based on study data in which applications were made with handwands, spraying below the waist as well as overhead. The UEs for fruit tree scenario are based on lognormal distribution as listed in Table I.D.3.
Application Rate	For all scenarios assessed, OPP used the maximum application rate to assess exposure (8 lbs ai/A was used for the fruit tree scenario).
Area Treated	For fruit trees, most of which are of the dwarf variety and therefore occupy relatively small areas, the area treated was entered as a uniform distribution (minimum 500 ft ² , maximum 1000 ft ²). The maximum value in this distribution was based on label restriction for applications made at the maximum rate (8lbs ai/A) for fruit tree applications.
Dermal Post-Application Exposure	
Residue	Chemical specific dislodgeable foliar residue data on olive trees (Klonne et al, 2000c) were used to assess dermal post-application exposure for this scenario. Statistical analysis of this data was performed and the initial residue concentrations were determined to be 0.0035 mg/ cm ² . Residue dissipation is based on the half-life of 7 days (as determined by the statistical analysis of the carbaryl olive DFR data).
TC	For the fruit tree scenario, the distribution of transfer coefficient was characterized as lognormal, with a mean of 940 cm ² /hour and a standard deviation of 260 cm ² /hour. The TCs were based on an apple pruning study. All transfer coefficients are based on individuals wearing short-sleeved shirts and short pants. A reduction factor was applied to account for body weights and surface area differences between adults and teenagers.
Duration	The time spent harvesting or performing post-application maintenance activities was represented by a uniform distribution ranging from 0.17 hour/day to 1 hour/day. These estimates of time spent in the garden performing post application activities (as well as the frequency of applications) were based on the ORETF survey (Johnson et al, 1999).
Ornamental Garden - Snail and Slug Bait Scenario	
Dermal and Inhalation Applicator Exposure	
Unit Exposure	The dermal and inhalation UEs for the methiocarb snail and slug bait scenario were based on study data for disulfoton applications to residential shrubs and flower beds (Merricks, 2001). The surrogate data consist of dermal and inhalation measurements of individuals using granular products. Specifically, the field study was conducted in Vero Beach, Florida. A total of 15 volunteers were monitored using passive dosimetry (hand/forearm wash solutions and personal air monitors). Application of the product was made by pouring the granules into the measuring cup/lid attached to the product package, and then distributing the granules onto the soil around the base of a shrub or onto a flower bed. The granules were then soil-incorporated with a garden rake. Each volunteer applied granular disulfoton around shrubs while wearing gloves and then again without gloves. Exposure data from the 15 replicates who did not wear gloves were reported. A lognormal distribution with a mean of 0.23 mg/lb ai, a standard deviation of 5.8 mg/lb ai, and maximum value of 3.4 mg/lb ai (representing the estimated 99th percentile of the lognormal distribution) was used to assess dermal exposure. A single point estimate of 0.00001 mg/lb ai (1/2 LOQ) was used for the inhalation UE since all measured



	values for inhalation were non-detects.
Application Rate	The application rate used in this assessment is based on the maximum label application rate of 0.2 lbs ai/1000 ft ² .
Area Treated	The area treated was entered as a uniform distribution of 10 to 2000 ft ² ; these dimensions are based on data from the National Gardening Association Survey (Johnson et al, 1999) and professional judgment. The low value of 10 sq ft was based on the label direction for treating small areas. The high value for ornamental bed size was determined by estimating the perimeter of 2200 ft ² house. It is assumed that the majority of ornamental beds are located around the perimeter of the house.
Pet Collar Scenarios	
Dermal Post-Application Exposure	
Residue	The fur residue concentration for the pet collar assessment is based on the amount of active ingredient in the respective pet collars and Agency default assumptions from the OPP SOPs for Residential Exposure Assessment (USEPA, 1997b). The residue values for carbaryl and propoxur are 0.00012 and 0.000069 mg/ cm ² , respectively. Residues were assumed to be available on a daily basis since pet collar products are designed to emit residues throughout their active period (120 days for carbaryl and 180 days for propoxur).
TC	The transfer coefficients used in the dermal post-application exposure assessment was derived from a groomer exposure study (Mester, 1998b) in which sixteen different veterinary personnel treated/handled eight dogs each, over a two to five hour time period. In this assessment, the transfer coefficients for adults and children were derived assuming an average transfer efficiency of 2.97% from the previous OP pet fur residue transfer efficiencies. For the revised NMC CRA, the data were used directly to generate an empirical distribution for the dermal transfer coefficient. The selected TCs ranged from 180 to 4700 cm ² /hour for adults and from 66 to 1800 cm ² /hour for children. These empirical distributions were used for both pet collar scenarios.
Duration	The time spent in this activity was assumed to follow a triangular distribution with minimum value of 0.03 hours, and a maximum value of 1.03 hours per day (Freeman et al, 2001). As part of this study, macroactivity and microactivity data were collected via questionnaires and videotaping of 19 children (aged 3 to 12) for a four hour period. The videotapes from the observational portion of this study were analyzed to determine frequency of contacts for several mouthing behaviors, as well as duration of time each child spent in various locations around the home. The results of this study include several measurements for the duration of time the observed children spent with their pets.
Oral non-dietary Post-Application Exposure	
Initial Hand Loadings	Hand loading (HR/2) is based on loading concepts used in SHEDS and CARES. The initial amount of residue available on the hand is determined as a percentage of total dermal exposure. The EPA Exposure Factors Handbook indicates that the surface area of the hands is approximately 6% of the total surface area of the body for children age 4 and under; 5% for children age 5 and over (USEPA, 2002c). The algorithm assumes mouthing one hand at a time, therefore, hand loading residues are divided by 2.
Frequency of mouthing events	The estimates of mouthing frequency were derived from several exposure studies and observational studies. For the pet collar scenario, hand-to-mouth events per hour were based on indoor frequencies as defined by a Weibull distribution (mean = 13 events/hour, standard deviation = 18). The distribution for frequency of hand-to-mouth events for indoor exposures, provided by ORD's Dr. Jiaping Xue, was calculated using the same methodology used to determine the frequency of mouthing events for



	outdoor exposures that was used in the lawn care assessment.
Surface Area Mouthed	The revised NMC CRA relied on Zartarian's (2003) analysis of surface area of hand mouthed. The analysis used the Leckie, et al, 2000 data to determine the fraction of the hand mouthed. The fraction of hand mouthed values were fit with a beta distribution (mean = 0.13 events/hour, standard deviation = 0.06).
Saliva Extraction Factor	To address the removal of residues from the hands by saliva during mouthing events, several studies were considered. The removal efficiency of residues on hands by saliva and other substances (e.g., ethanol) suggests a range of removal efficiencies (Geno et al., 1995; Fenske and Lu 1994; Wester and Maibach 1989). Based on the above studies, a uniform distribution of 20% to 50% was used in this assessment for saliva extraction factors.
Duration	The duration of exposure values used for the non-dietary exposure assessment are the same as those used in the dermal post-application assessment for the pet collar scenarios presented above.
Golf Course Scenario	
Dermal Post-Application Exposure	
Residue	Since liquid broadcast applications to golf course turf are permitted, the liquid TTR data (Mester, 1999) used to assess post-application exposure for the golf course scenario. Statistical analysis of this data was performed and an initial concentration of 0.00065 mg/ cm ² was calculated and used in this assessment. Dissipation is based on a 3.6 day half-life. For details of the statistical analysis see Appendix II.D.2.
TC	The surrogate data used to derive transfer coefficients were based on two measurements of four individuals playing golf on two golf courses treated with chlorothalonil (Ballee, 1990), and the exposure of golfers (four volunteers) to flurprimidol (Moran et al, 1987). For both studies, an assumed transfer efficiency of 1% was used to calculate the transfer coefficients, since the studies were conducted using sprayable formulations. Based on these two studies, a lognormal distribution with a mean of 480 cm ² /hour and a standard deviation of 160 cm ² /hour was used to represent the transfer coefficient. This distribution was truncated at the calculated 99th percentile value of 960 cm ² /hour. All transfer coefficients are based on individuals wearing short sleeved shirts and short pants. A reduction factor was applied to account for body weight and surface area differences for adults and teenagers.
Duration	The exposure duration for individuals playing golf was assumed to be a uniform distribution bounded at the low end by two hours and at the upper end at four hours. The four-hour value was obtained from the CGCM survey.



E. Cumulative Risk from NMC Pesticides in Drinking Water

1. Introduction

The Food Quality Protection Act (FQPA) of 1996 requires the Agency to assess the risks from different pesticides having a common mechanism of action, focusing on the likelihood that a person will be concurrently exposed to multiple pesticides from multiple sources (food, drinking water, and residential uses). Ideally, data to support the drinking water portion of this exposure assessment would consist of information on multiple pesticides and their transformation products, collected from sufficient drinking water sources throughout the U.S. and at a sufficient frequency to reflect the range in spatial and temporal patterns of pesticide occurrence in water. The great diversity of geographic-, climatic-, and time-dependent factors that affect the levels of pesticide residues in water creates unique challenges in characterizing drinking water exposure. EPA's Office of Pesticide Programs (OPP) must rely on both available monitoring data and modeling to develop sufficient data for use in the exposure assessment.

The Agency used the same methods for estimating surface water exposure in the revised NMC CRA as it did in the OP CRA (USEPA, 2002b; FIFRA SAP, 2002) because of similarities in use (both NMCs and OPs are insecticides), hazard endpoints (ChE inhibition occurring in the acute- or short-term), and exposure requirements (estimates of peak concentrations and time-series distributions).

Unlike the OP pesticides for which surface water is the likely source of concern for drinking water, the NMCs also are likely to reach ground-water sources of drinking water. The Agency presented a conceptual model for ground water exposure and a plan for evaluating the capability of three ground water models to estimate NMC concentrations to the FIFRA SAP in February, 2005. Based on feedback from the SAP (FIFRA SAP, 2005a), EPA followed up with a revised conceptual model and analysis plan using one of the models evaluated in the preliminary assessment (FIFRA SAP, 2005b).

The revised NMC CRA follows the same approach as outlined in the preliminary assessment (USEPA, 2005b), and includes several additional ground water exposure scenarios to further capture the range of high leaching potential areas in high NMC use areas, as well as a more representative assumption for the depth to groundwater. Based on analysis of additional monitoring data, the Agency has been better able to identify the specific conditions that are likely to result in high NMC



exposure in private drinking water wells and to better characterize the spatial extent of potential high NMC exposure areas.

In addition, the reported cumulative NMC exposures in this section reflect the revised relative potency, inter-species, and FQPA safety factors documented in the Hazard chapter (I.B) of this revised assessment.

2. Problem Formulation

Pesticide concentrations found in drinking water are not random, but are in large part determined by the amount, method, timing and location of pesticide application, the physical characteristics of the watersheds and/or aquifers in which the community water supplies (CWS) or wells are located, and other environmental factors, such as rainfall, which can cause the pesticide to move from the location where it was applied.

a. Drinking Water Exposure Needs for the NMC Cumulative Assessment

For the NMC group, the toxicity endpoint of concern results from short-term exposure (acute effects). To adequately characterize the potential impacts of pesticide residues in drinking water, the estimated residue concentrations need to reflect a sufficient frequency in time to capture peak concentrations. Because pesticide loads in surface water tend to move in relatively quick pulses in flowing water, frequent sampling is necessary to reliably capture peak concentrations for surface water sources of drinking water. Pesticide concentrations in ground water are generally the result of longer-term processes and less frequent sampling can sufficiently characterize peak ground water concentrations.

The drinking water exposure assessment needs to account for the potential for any or all of the NMC residues included in the cumulative assessment group ([REF _Ref175716149 \h]) to occur together in drinking water sources. To realistically estimate exposures, the assessment must take into account those factors (crop uses, pest pressures, timing of application, etc.) that determine whether more than one NMC pesticide can occur together in time and place. Although multiple NMC pesticides may be registered for use on the same crop, they may not necessarily be used at the same time. Monitoring data could provide real-time estimates of co-occurrence but needs to account for all of the potential NMCs used in the monitoring area, be of sufficient frequency to capture short-term peaks in pesticide exposure, particularly in surface water, and span sufficient years to capture the impact of variability in use and weather patterns on pesticide transport.



Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. NMC use patterns and availability of national monitoring data

Pesticide	Use pattern likely to result in water exposure?	Availability of national water monitoring data?
Aldicarb (including sulfoxide, sulfone degradates)	Yes (agricultural uses)	Yes: NAWQA, Reservoir monitoring; state monitoring; registrant studies
Carbaryl	Yes (agricultural and residential uses)	Yes: NAWQA, Reservoir monitoring; registrant studies
Carbofuran (including 3-hydroxycarbofuran)	Yes ¹ (agricultural uses)	Yes: NAWQA, Reservoir monitoring; state monitoring
Formetanate HCl	Yes (agricultural uses)	No
Methiocarb	Insignificant impact from limited use	Some limited NAWQA monitoring
Methomyl	Yes (agricultural uses)	Yes: NAWQA, Reservoir monitoring
Oxamyl	Yes (agricultural uses)	Yes: NAWQA, Reservoir monitoring
Pirimicarb	Insignificant impact from limited use	No
Propoxur	No (indoor uses; voluntarily cancelled)	Some limited NAWQA monitoring
Thiodicarb (including methomyl degradate)	Yes (agricultural uses)	No

¹ EPA proposed to cancel all domestic uses in 2006 IRED, in which case exposure would not be likely

b. Nature of NMC Exposure in Drinking Water Sources

This section briefly summarizes the nature of expected NMC exposure in drinking water sources based on individual chemical assessments, available water monitoring data, and published literature on the potential impact of conventional drinking water treatment processes on NMCs in water.

Re-registration eligibility documents (REDs), interim REDs (IREDs), drinking water assessments, or ecological risk assessments are available for all of the NMC pesticides in Table I.E.1 except for pirimicarb (USEPA, 1997c, 1997d, 1999f, 2003a, 2005c, 2005d, 2005e, 2006c, 2006d, 2007b, 2007d, 2007e).

Seven NMC pesticides – aldicarb (including its sulfoxide and sulfone degradates), carbaryl, carbofuran, formetanate HCl, methomyl, oxamyl, and thiodicarb – have the potential to reach surface and/or ground water sources of drinking water based on use and chemical fate and transport properties. Propoxur has been detected in a few, predominantly non-agricultural monitoring sites in the US Geological Survey (USGS) National Water Quality Assessment (NAWQA) monitoring program (Appendix II.E.1). However, the current indoor uses are not expected to contribute to the NMC cumulative load in drinking water sources. When the Agency gathered usage information on the



NMC pesticides for the regional cumulative drinking water exposures, usage of methiocarb and pirimicarb were of such a limited extent that they did not factor into the NMC cumulative exposure for drinking water (see Appendix II.E.4). These pesticides were not used in areas of high combined NMC use identified in the regional assessments described below.

The individual chemical assessments indicate that the NMC pesticides are likely to reach surface water sources of drinking water via runoff or sediment transport, and have been detected in monitoring studies. Two carbamates – aldicarb and carbofuran – are likely to reach and persist in ground water sources of drinking water, especially in shallow, acidic aquifers. Three other carbamates – carbaryl, methomyl, and oxamyl – may also reach ground water, but are not likely to persist.

The most extensive source of national water monitoring data for pesticides is the USGS NAWQA program, which includes seven of the carbamates in its list of pesticides ([REF _Ref175717773 \h]). The NAWQA program focuses on ambient water rather than on drinking water sources, is not specifically targeted to pesticide use areas, and is sampled at a frequency (generally weekly or bi-weekly during the use season) not sufficient to provide reliable estimates of peak pesticide concentrations in surface water. However, the program provides a good understanding on a national level of the expected occurrence of pesticides in flowing water bodies that may be representative of drinking water sources. The monitoring data are better indicators of the nature of occurrence of pesticides with widespread use rather than of pesticides that are limited to a few crops or pests. USGS (2004) provides a detailed description of the pesticide monitoring component of the NAWQA program.

A summary of the first cycle of NAWQA monitoring from 1991 to 2001 indicates that the seven NMC pesticides were not frequently detected in the NAWQA study units ([REF _Ref175717773 \h]). Carbaryl and carbofuran were the most frequently detected NMC pesticides in streams and ground water, reflecting the broader use patterns of these particular insecticides. In most instances, maximum reported detections of the NMC pesticides were in the single parts per billion or sub-parts per billion range.

As expected, co-occurrence of NMC pesticides in monitored water samples reflects use patterns and overall intensity of use. Carbaryl and carbofuran are the most common NMCs occurring together in the NAWQA sampling; up to three different NMCs have been detected in the same surface water samples in the NAWQA study units. Although less commonly observed, more than one carbamate was also detected in a



small number of ground water samples. More detailed summaries of the USGS NAWQA monitoring data can be found in Appendices [REF _Ref178099759 \r \h] (surface water monitoring) and II.E.2 (ground water monitoring).

Table I.[STYLEREF 2 \s]-[SEQ Table * ARABIC \s 2]. Summary of carbamate detections in the USGS NAWQA study, 1991-2001 (provisional data published by USGS in 2003)

Pesticide	Agricultural Land Use			Mixed Land Use			Urban Land Use		
	% detect	Max ug/L	95th %ile	% detect	Max ug/L	95th %ile	% detect	Max ug/L	95th %ile
Surface Water Monitoring (Martin et al, 2003)									
Aldicarb	0.2%	0.5	nd	0%	Nd	nd	0%	Nd	nd
Carbaryl	9.2%	5.2	nd	15.4%	0.5	nd	43.8%	5.2	0.3
Carbofuran	9.6%	7.0	0.04	3.3%	0.7	nd	2.1%	0.1	nd
Methiocarb	0.1%	0.1	nd	0%	Nd	nd	0%	Nd	nd
Methomyl	1.6%	0.7	nd	0.3%	0.3	nd	0%	Nd	nd
Oxamyl	0.8%	0.2	nd	0%	Nd	nd	0%	Nd	nd
Propoxur	0.2%	0.1	nd	0.2%	0.2	nd	0.2%	0.3	nd
Ground Water Monitoring (Koplin and Martin, 2003)									
Aldicarb (incl.degradates)	0.3%	1.8	nd	0.1%	0.1	nd	0%	Nd	nd
Carbaryl	0.4%	0.02	nd	0.8%	0.5	nd	1.6%	0.03	nd
Carbofuran	1.6%	1.3	nd	0.4%	0.2	nd	0.7%	0.09	nd
Methiocarb	0%	nd	nd	0.1%	0.03	nd	0%	Nd	nd
Methomyl	0.1%	0.04	nd	0.1%	0.1	nd	0.2%	0.4	nd
Oxamyl	0.8%	2.1	nd	0.1%	0.03	nd	0.2%	0.3	nd
Propoxur	0.1%	0.06	nd	0.1%	0.06	nd	0.2%	0.3	nd

NAWQA and other surface-water monitoring programs show that pesticide concentrations in surface water are highly variable in location and in time. This is particularly true for insecticides, such as the NMCs, where usage is often in response to specific pest pressures which are likely to be concentrated in some areas but not in others and in some years but not necessarily every year. In addition to variable use patterns, NMC concentrations in surface water are influenced by local soil, hydrology, and weather patterns and by the timing of rainfall events in relation to pesticide use.

In 2001, The U.S. Department of Agriculture (USDA) expanded its Pesticide Data Program (PDP) to include drinking water. Over the following three years, between 21 and 36 surface water systems were monitored, the majority of which were located in California and New York. Sampling frequency varied from site to site, but was no more frequent than two times a month. Treated (finished) water samples were collected at different locations at different times; several NMC chemicals were included in the analyses. Several NMC compounds (carbaryl, carbofuran, and oxamyl) were found in finished drinking water at a number of sites. Concentrations found were low, none exceeding 80 ppt.



The magnitude of these detections can be interpreted as a minimum exposure level at these sites, but cannot be interpreted to be representative of overall exposure. Given the site to site variability in factors associated with pesticide exposure, limited frequency of sampling, and limited number of sites, the study cannot be used to represent national exposure to pesticides in finished drinking water. Monitoring is most representative of sites sampled in California and New York. More information on the results can be found in Appendix II.E.1.

Aldicarb is the NMC that has been the focus of the most extensive monitoring in water resources. While aldicarb has not been detected frequently or in high concentrations in ground water in the NAWQA program, extensive targeted monitoring by others (registrant, state and local governments, universities – see Appendix II.E.2) shows that, under certain conditions, aldicarb residues (parent and degradates) can occur in ground water and private wells at concentrations as high as several tens to several hundred parts per billion ($\mu\text{g/l}$).

The frequency and magnitude of detection of aldicarb residues in ground water is dependent not only on pesticide use but also on the leaching potential of the overlying soil and vadose zone and, for the sulfoxide and sulfone transformation products, the pH of the soil and ground water. For example, while no aldicarb residues were detected in ground-water monitoring conducted by the USGS in the Biscayne and surficial aquifers of southern Florida (McPherson et al, 2000), roughly one-third of the monitoring wells located under citrus groves in the central ridge of Florida had detections of aldicarb residues (USGS, 2006). Monitoring data for private wells collected by the state of Florida showed few detections of aldicarb residues (<2% of wells sampled). However, the detections, as high as $47\mu\text{g/l}$ were clustered along the central ridge in the vicinity of citrus groves (FLDEP, 2005).

Label changes for aldicarb now restrict use from certain areas (such as the northeastern states and Wisconsin) and add well-setbacks in other areas. In addition, total aldicarb residues (primarily the sulfoxide and sulfone transformation products) can persist in ground water for years or decades after use. Twenty years after aldicarb use on Long Island, NY, was halted, aldicarb residues are still the most frequently detected pesticide compounds in ground water in Suffolk County (Suffolk County Dept. of Health Services, 2000).

A recent survey of private wells by Bayer CropScience (MRIDs 46793701, 46793702, 46793703, 46793704, 46793705, 46793706) found aldicarb residues – predominantly sulfoxide and sulfone metabolites – in 10 percent of the wells sampled, with the greatest frequencies of detections in the Southeastern US (16%, with a maximum



detect of 2.9 ug/L) and the Mississippi Delta (9%, with a maximum detect of 2.6 ug/L) regions. Aldicarb detections showed a regional pattern, with this highest frequency of detects in Alabama (22%) and South Carolina (21%) in the Southeast region and southeastern Missouri/northeastern Arkansas (23%) in the Mississippi Delta region. Because the detections come from a single sample, the concentrations should be compared against median concentrations from a distribution of ground water concentrations over time (USEPA, 2007a).

Carbofuran was another NMC for which extensive monitoring has occurred; however, the extent of ground water monitoring has decreased significantly in the last decade, so current impacts are not as well documented. Several inferences can be drawn from the body of available data on carbofuran. Targeted ground water monitoring studies show a clear pattern of carbofuran movement into ground water, with maximum detections in the same range as that reported for aldicarb. Because transport to ground water typically takes longer than transport to surface water, measured concentrations of carbofuran in ground water, especially in deep groundwater, may represent usage that occurred years before the samples were collected. As with aldicarb, carbofuran will also persist in ground water for long periods of time after use has been discontinued. This is particularly true for acidic ground water because carbofuran is stable to hydrolysis (the major route of degradation in ground water) at pH values of 6.0 or less.

EPA's review of available laboratory studies and monitoring data indicates that conventional water treatment processes such as coagulation, sedimentation, and conventional filtration will not reliably remove or transform the NMCs in drinking water sources (Appendix II.E.3). This is further substantiated by USDA PDP monitoring that shows detections of NMC residues in finished/treated water samples (Appendix II.E.1). Lime softening and activated carbon filtration can be effective in removing the NMC pesticides. With the exception of parent aldicarb, lime softening processes will break down NMC pesticides through alkaline-catalyzed hydrolysis. Sorption on activated carbon by granular activated carbon (GAC) or powdered activated carbon (PAC) appears to be at least partially effective in removing NMCs from drinking water (percent removal ranges from 20 to 38% for aldicarb and oxamyl to 60 to 80% for carbofuran, carbaryl, and methiocarb). Other treatment methods, such as chlorination, chloramination, chlorine dioxide, and potassium permanganate, are only effective in oxidizing NMC compounds containing a methylthio group ($\text{CH}_3\text{-S-}$), e.g., methiocarb and aldicarb. These compounds are expected to oxidize to sulfoxide and sulfone carbamates that hydrolyze rapidly at alkaline pH values. The Agency estimates that lime softening is used on 7% or less of community ground water systems serving populations of 10,000 or less and less



than a third of systems serving more than 10,000 people (USEPA, 2001b). Carbon filtration is used on less than half of the large community water systems, with decreasing percentages of smaller systems using GAC or PAC (USEPA, 2001b).

c. Summary

The goal of the NMC drinking water exposure assessment is to provide estimates of distributions of NMC residues (concentrations in drinking water) that account for:

- daily and seasonal variations in residues over time associated with time of application(s) and runoff/leaching events (surface water concentrations are expected to be more variable in time than ground water concentrations)
- year-to-year variations related to weather patterns, pest pressures, and use
- variability in residues from place to place, resulting from the source and nature of drinking water and from the regional / local factors (soil, geology, hydrology, climate, crops, pest pressures, usage) that affect the vulnerability of those sources
- the potential for co-occurrence of more than one NMC in location and time only when this is likely to happen

3. Conceptual Model

Risk is a function of both hazard and exposure, and estimation of the exposure portion for drinking water requires data on concentrations of the pesticides in the drinking water and consumption of drinking water for different demographic populations. Drinking water is locally derived and concentrations of pesticides in source water fluctuate over time and location for a variety of reasons. Pesticide residues in water fluctuate daily, seasonally, and yearly as a result of the timing of the pesticide application, the vulnerability of the water supply to pesticide loading through runoff, spray drift and/or leaching, and changes in the weather. Concentrations are also affected by the method of application, the location and characteristics of the sites where a pesticide is used, the climate, and the type and degree of pest pressure.

While monitoring data provide a picture of the occurrence of NMC pesticides in drinking water resulting from variable use in selected locations, monitoring data alone are not sufficient for the NMC cumulative drinking water exposure assessment, due to the spatial and temporal scale of monitoring networks. This section describes the approach used to estimate cumulative NMC residues in drinking water using models, to ensure that peak concentrations from registered uses

Based on the needs of the probabilistic cumulative exposure assessment and the information from monitoring data, OPP designed a drinking water assessment that provides multiple years of daily residue concentrations from drinking water sources in regions where high NMC use coincides with vulnerable drinking water sources. While the available monitoring studies were not designed to provide data for a multi-chemical drinking water exposure assessment and were not of sufficient frequency to provide a time series for use in a probabilistic exposure assessment, the data were used to make sure that estimated exposures from modeling were within the same range or that any discrepancies could be explained.

Drinking water exposure will vary locally as a result of pesticide use, agricultural practices, the nature and vulnerability of drinking water sources, and weather patterns. Thus, the water exposure assessment focused on specific geographic areas of relatively high NMC use in a manner that would be realistically protective of all NMC use areas. To facilitate the regional screening approach, the Agency adapted a modification of the USDA Farm Resource Region map (Heimlich, 2000) as a framework for identifying one or more locations which represent an area of the greatest concern for drinking water exposure in each region ([REF_Ref175717320 \h * MERGEFORMAT]). In this way, the Agency chose a set of locations to represent vulnerable drinking water sources throughout the U.S.

RPF-adj NMC Use, lb/cy

- ◻ NMC Cumulative Regions
- ▨ Surface Water Scenario Locations
- Ground Water Scenario Locations

<2,500
 2,500-25,000
 25,000-50,000
 >50,000

NMC Central WA
 NMC Central N.H.
 NMC Northeast
 NMC Central IL
 NMC Central KS
 NMC East PA
 NMC Delaware
 NMC H.C. Coastal Plains
 NMC H.C. and H.C.
 NMC East GA
 NMC GA Coastal Plains
 NMC H.C. and FL
 NMC FL Central Ridge
 NMC South FL



drinking water exposure sites

OPP selected Locations where NMC residues in drinking water sources are likely to be of greatest concern based on:

- **Relatively high NMC use:** both total NMC use by county and relative potency-adjusted NMC use were considered; for ground water sources, EPA also looked at the areas with the highest aldicarb and carbofuran uses;
- **Nature and source of drinking water:** EPA used the USGS report on water use in the U.S. (USGS, 1998, 1999) to identify the drinking water sources (public surface water, public ground water, domestic private) by county and information on surface water intake locations to identify the dominant drinking water sources in high NMC use counties;
- **Vulnerability of the drinking water sources:** vulnerability of surface water sources was based on the relative runoff potential of the watershed area around surface water intakes; vulnerability of ground water sources was based on the leaching potential of the overlying soils and vadose zone.

For each region, the Agency used the estimated NMC cumulative distribution from the vulnerable water source to represent the drinking water portion of the dietary exposure estimate for the entire region. If NMC levels in water from these vulnerable sites are not major contributors to the total regional cumulative exposure, then the Agency can reasonably conclude that drinking water exposures will not be a concern in other less vulnerable areas in that region. If drinking water exposure from one or more of these vulnerable sites is a significant contributor to the total cumulative exposure, then additional evaluations may be necessary to characterize the extent of the potential exposure.

For the cumulative assessment, the Agency considered exposure from both surface- and ground-water sources of drinking water. In both cases, the Agency simulated potential exposure to sensitive populations in a geographic sense. Surface-water sources of water consisted of source water from small reservoirs in predominantly agricultural watersheds with high NMC use. Ground-water sources of water were shallow private wells located in highly permeable soils in high NMC use areas.